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EDITORIAL

ETHICS AND THE ANNOUNCEMENT OF SPECIALTY PRACTICE

In the October, 1960, issue of Oral Surgery, Oral Medicine and Oral Pathology, an editorial advised persons interested in the field of oral radiology to withhold specialty status demands until the specialty had been developed more fully in breadth and depth of knowledge, in research activities, and in the number of persons whose principal interest lies in this very important phase of dentistry. There seems no reason to change this attitude.

A review of the *Principles of Ethics* of the American Dental Association, specifically Section 18—"Announcement of Specialty Practice," raises certain questions about persons whose past and present professional activities place them in the category of a nondesignated specialty; they certainly cannot be classed as general practitioners of dentistry. This editorial will confine itself to dentists practicing oral roentgenology exclusively. It is pertinent, however, to emphasize that these remarks apply to other nondesignated specialty groups as well.

Section 18 states that the indicated area of dentistry must be "one for which there is a certifying board approved by the American Dental Association." If this portion and one or more other paragraphs of Section 18 cannot be met, the dentist is denied the use of the words "specialist," "specializing in," or other similar descriptions in directory listings. What is to be done about the dentist who for the past number of years has been practicing oral roentgenology exclusively? Let us arbitrarily use a period of fifteen years as an example. This man is well versed in the techniques of the science and in its interpretative phases. He has been rendering service and giving advice during this period of time. *He is doing nothing other than specializing.* Is the American Dental Association within its rights in declaring this person unethical because he continues to announce in public directories the fact that the only service he offers is restricted to this field, that his competencies are centralized in this area, and that he truly specializes in oral roentgenology?

It is entirely possible that through such action the American Dental Association will deprive one or more of its members of their livelihood. How else,

other than making his competencies known, can this person maintain and further develop his chosen professional activity? It is true, and the fact can be substantiated, that the services rendered in the offices of those who specialize in the techniques and interpretation of oral roentgenology are superior to the roentgenologic services offered in the average dental office. The public should have the opportunity of securing service from these ethical practitioners. To call such persons "unethical" because they refuse to discontinue their policy of making their competencies known to the professional and lay public is ridiculous.

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SUBLINGUAL CYST

Report of a Case

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A RELATIVELY large retention cyst that occurs in the floor of the mouth, generally between the root of the tongue and the mandible, is the ranula. It is caused by obstruction of the ducts of the small sublingual glands and, more rarely, the submaxillary glands, which results in retention of their secretions.[1] There is no pain associated with the cyst, but there may be an elevation of the tongue, impairing both mastication and speech.

These cysts vary in location and size. They may be located superficially or deep. When superficial, they are generally thin walled and bluish in color, whereas the deeper cysts have thicker walls and are more normal in color. Thoma[2] states that these cysts may become displaced posteriorly past the mylohyoid muscle and enter the submandibular area. In this region they are known as sublingual cysts.

The following case illustrates the potential of a sublingual cyst to form a large swelling in the floor of the mouth as well as to protrude into the submandibular area and be externally apparent.

CASE REPORT

An 8-year-old Indian girl came to the oral surgery clinic on Oct. 13, 1959, complaining of a swelling in the left floor of the mouth and submandibular area.

History of Present Illness.—The patient's mother stated that the swelling in the floor of the mouth was first noticed in June, 1959. No pain was associated with the swelling, but the tongue was becoming slightly elevated. The patient was taken to her local physician, who incised and drained the area three times during June and July. Each time the swelling recurred. The patient's mother said that in August, 1959, a swelling also became evident under the left jaw and that it progressively enlarged.

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Past History.—The patient's past history was essentially negative. She had had no serious illness, and there was no history of previous surgical procedures.

Head and Neck Examination.—Intraorally, there was a large, fluctuant, nontender, noninflammatory swelling in the left floor of the mouth, which caused the tongue to be elevated (Fig. 1). The mucous membrane was taut and bluish in color. There was no

Fig. 1.—Preoperative view showing large swelling in the floor of the mouth.

Fig. 2.—Preoperative view. Note diffuse swelling in the left submandibular region.

apparent involvement of Wharton's duct. The teeth were relatively free of caries and in satisfactory occlusion. Extraorally, there was a diffuse, soft, nontender swelling in the left submandibular region (Fig. 2). Upward pressure in this area caused the swelling in the floor of the mouth to be elevated.

Tentative diagnosis: Sublingual cyst.

Physical Examination.—The patient was an obese, well-developed, well-oriented girl who appeared to be in no distress. The blood pressure was 123/75; the pulse rate was 90 and regular; and the temperature was 99.0° F. The heart and lungs were considered normal. Laboratory examinations, urinalysis, and a complete blood count were within normal limits.

Fig. 3.—Anteroposterior roentgenogram. Note contrast material beneath the left mandible.

Roentgenographic Examination.—Periapical and occlusal roentgenograms were normal, as was a sialogram of the left submaxillary gland. An 18-gauge needle was attached to an aspirating syringe and inserted into the cyst intraorally. About 5 ml. of a stringy, brownish, mucoid fluid was aspirated. Contrast material was then injected into the cyst. Lateral jaw and anteroposterior roentgenograms demonstrated a large multiloculated cyst that extended beneath the left mandible (Fig. 3).

Treatment and Course.—On Oct. 15, 1959, the patient was given premedication consisting of Nembutal sodium, 50 mg. (two hours preoperatively), Demerol hydrochloride, 50 mg., and scopolamine, 0.2 mg. (one and one-half hours preoperatively).

After the patient had been given Pentothal sodium and nitrous oxide–oxygen nasotracheal anesthetic, the face and oral cavity were prepared with surgical soap and aqueous Zephiran chloride solution and the patient was draped with sterile towels.

Because of the obvious extent of the cyst, we decided upon a modified marsupialization procedure by which we planned to enucleate as much of the superior portion of the cyst lining as possible, remove any glandular tissue that might be involved, and then pack the cavity open with an iodoform dressing.

A small probe was first passed into the left Wharton's duct, outlining its course. Then an intraoral incision was made over the top of the cyst, extending about 4 cm. in a posteroanterior direction. By blunt dissection, the overlying mucous membrane was separated from the cyst. While being grasped with Allis forceps, the cyst was ruptured, releasing a large quantity of brownish mucoid material which was removed with the aspirator. By careful

dissection, the cystic lining was separated from Wharton's duct and the lingual nerve. Several sublingual glands were found to be entangled within the cyst lining, and these were also removed. After the resulting cavity was irrigated with saline solution, the cyst was found to extend posteriorly and below the mylohyoid muscle. Two additional compartments were located deep, but these were found to be in direct continuity with the main cavity. All of the cystic lining that had been dissected free was removed, leaving only the main base and the two compartments covered with cyst lining. The cyst cavity was then packed open with

Fig. 4.—Appearance three months following surgical removal of cyst.

about 2 feet of ½ inch iodoform gauze saturated with balsam of Peru and mineral oil. Two 000 black silk sutures were loosely placed to maintain the dressing in position. The patient tolerated the entire procedure well and left the operating room in a satisfactory condition.

Postoperatively, an ice bag was applied intermittently to the left submandibular area and the patient was instructed to hold ice chips in her mouth on the day of the operation. A high-protein liquid diet with supplemental feedings was ordered. Demerol hydrochloride, 30 mg. every four hours as required for pain, was prescribed. The patient had received Achromycin, 250 mg. every six hours, for two days prior to the operation; this was continued postoperatively for seven days. On the first postoperative day the use of warm saline mouthwashes after each meal and at bedtime was started.

The postoperative course was uneventful. On both the fifth and sixth days following the surgical procedure about 6 inches of the dressing was removed. The patient was discharged from the hospital on the seventh postoperative day. On the day of discharge the sutures were removed, as was the remaining iodoform dressing. After the oral defect had been thoroughly irrigated with saline solution, a fresh dressing was placed.

The patient was seen in the oral surgery outpatient department on Nov. 3, 1959. The dressing was removed, the floor of the cystic cavity was irrigated with saline solution, and approximately 8 inches of fresh iodoform dressing was placed. At that time the cystic area had greatly decreased in size. Some swelling was still apparent in the left submandibular area. The patient returned to the clinic on Nov. 10, 1959, showing continued improvement. The dressing was removed and not replaced. In January, 1960, the patient was seen for the last time. The left floor of the mouth had completely healed, with a resulting normal contour, and there was no evidence of swelling in the submandibular region (Fig. 4).

Pathologist's Report.—

Macroscopic: The specimen consisted of an irregular group of firm, nodular, glandlike structures connected to a thin membranous lining, forming a mass which measured roughly 2.5 by 3 by 1 cm. Representative sections were submitted for histologic evaluation.

Microscopic: Microscopic examination revealed a thin-walled cyst with a lining of cuboidal cells, which in places became fairly flat. A part of the cystic lining was attached

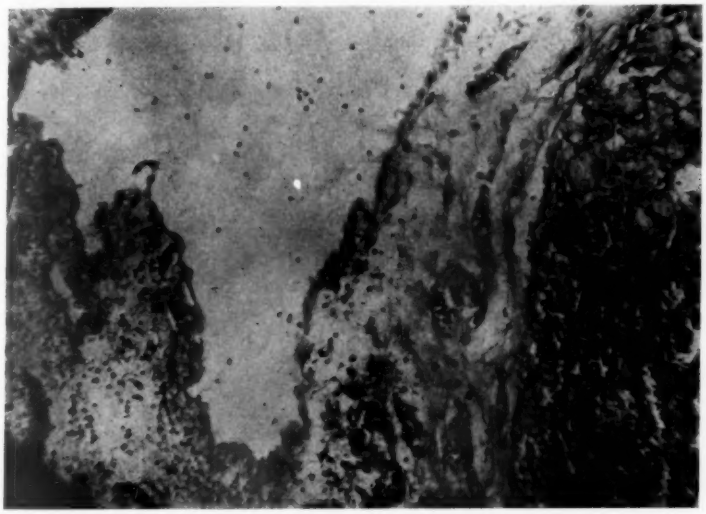

Fig. 5.—Photomicrograph showing attachment of the cystic lining to a mixed type of salivary gland.

to a mixed type of salivary gland with mucus-secreting elements predominating. Throughout the section there were scattered small foci of lymphoid tissue (Fig. 5). There was no evidence of malignancy.

DISCUSSION

Both the ranula and the sublingual cyst are subject to rupture when traumatized. If they are incised and drained, the fluid will reaccumulate when the tissue has healed. For this reason, one of several methods of treatment should be employed for an optimum result. Thoma[3] lists the following methods of treatment: (1) excision of the external surface of the cyst (marsupialization); (2) intraoral excision of the cyst and adjacent mucous gland; (3) extraoral excision of the cyst (deeply placed sublingual cysts).

In the case just reported a combination of two of the methods of treatment just listed was used with a satisfactory end result. A modified marsupialization was performed, along with removal of the involved sublingual glands.

This method is recommended for the removal of deeply situated sublingual cysts with oral manifestations when the lining is very friable and extremely difficult, if not impossible, to enucleate.

SUMMARY

A case in which a large sublingual cyst produced both intraoral and extraoral swellings is reported. The cyst was successfully treated by a modified marsupialization procedure and removal of the involved sublingual glands. This procedure appears to be indicated when deeply located cysts with extremely friable linings are approachable intraorally.

The authors wish to acknowledge the help of Dr. Paul W. Goaz in the preparation of this manuscript.

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Correction

In a recent article entitled "Oral Manifestations of Hereditary Hemorrhagic Telangiectasia" (ORAL SURG., ORAL MED. & ORAL PATH. 14: 550-555, May, 1961), Durocher, Morris, and Burket state that in a review of the literature they found that the first article on this subject in the "dental literature of the past forty-five years" was one by Scopp and Quart (ORAL SURG., ORAL MED. & ORAL PATH. 11: 1138, 1958). However, a review of the 1957 *Dental Index*, page 131, indicates that the first article was by H. M. Syrop (ORAL SURG., ORAL MED. & ORAL PATH. 10: 253, 1957.)

OPERATING ROOM DECORUM IN ORAL SURGERY

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BACTERIA are carried into wounds from the air as well as from skin surfaces and materials used during an operation. It is impossible to sterilize the oral cavity, but the use of a sterile technique and precautions for control of air-borne infections will reduce the possibility of introducing infectious bacteria into the wound.

Air-borne infection may arise from such sources as floor dust, ventilators and windows, shoe dirt, and air expired by operating room personnel. Wound infections have also been traced to the presence of bacteria in the air and on soiled operating tables, rubber pads, buckets, and restraining straps, not only in the early days of surgery but also under present standards and principles of aseptic technique. One must be aware of the fine films of dust visible on window sills and cabinet shelves; this dust has settled out from the air. Organisms increase on an aseptic field more rapidly when the operating room is occupied by people.

Maintaining asepsis sometimes means going to what may be considered extreme measures by those who do not understand the many possibilities of accidentally introducing infection. Physical sterilization of the air has not been technically justified for general operating room use. At present it is more important to stress the reduction of infection by the development of perfect techniques and absolute cleanliness in the operating rooms. Therefore, in the interest of protecting the patient from infection and maintaining the best decorum, both in the operating room and in the outpatient oral surgery clinic (Figs. 1 and 2), all personnel should endeavor to observe the best operating room standards, as follows:

1. Operating room personnel should not be on duty while suffering from nasopharyngeal infections.

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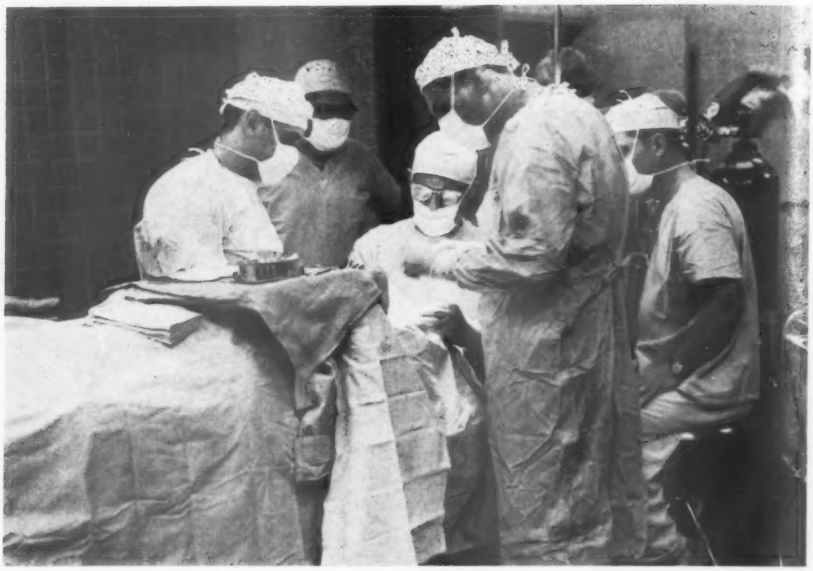

Fig. 1.—Decorum in the oral surgery operating room of the Research and Educational Hospitals, Chicago, Illinois.

Fig. 2.—Decorum in the outpatient oral surgery clinic of the University of Illinois, Chicago.

2. The nose and mouth of everyone in the operating room should be adequately masked at all times. Masks should not be removed between operations but should be worn by all personnel until every procedure on the day's schedule has been completed.

It is a good rule, particularly in rooms used for orthopedic surgery, for all personnel to wear two masks to cover the mouth and nose. Some hospitals are using double masks in all operating rooms.

Interested guests and students may circulate considerable bacteria by getting too near the field of operation. When a sneeze or cough is unavoidable, the person should leave the field and turn the head away from the sterile gown and gloved hands. Sometimes it is best to change gloves and gown to avoid contamination of the field.

Organisms are spread by coughing, sneezing, talking, and sighing. Therefore, a person with an upper respiratory infection should never enter the operating room.

3. The hair should be clean and free of dandruff. The hair and head should be completely covered by a cap or turban. No hair should protrude from beneath the cap.

4. The hands should be scrubbed carefully with hexachlorophene soap for five minutes before the first operation of each day and for three minutes before each subsequent operation.

5. Out of consideration for the patient who is awake, unnecessary talking in the operating room and loud noises in the halls should be avoided. Doors to operating rooms should be kept closed whenever an undraped patient is awake.

6. The towel used for drying the arms should not touch the clothing. Drying should always proceed from the hands upward toward the elbows. A different half of the towel is used for each hand, and then the towel is discarded.

7. To prevent contamination after initial scrubbing, one should always keep the hands above the level of the elbows, so that water cannot run down over them from the elbows. After the gown and gloves have been put on, the hands must be kept above the waist and covered with a towel or a glove wrapper until the operation is begun. At the operating table the hands should always be kept on the drapes.

8. The circulating and instrument nurses should watch for perspiration on the faces of the operating team, as the mask does not catch these droplets. The perspiring person should turn the head to one side while the circulating nurse wipes the perspiration from the forehead or glasses without contaminating his gown, his gloves, or the surgical field.

9. Patients with highly infectious gas bacilli or tetanus organisms should not be operated upon in the main operating room. Operations on these patients should be scheduled to follow all clean procedures and should be performed in the septic operating room.

It is required that those who have assisted with a contaminated case rescrub the hands and arms for ten minutes before assisting with a clean case.

We might add to this list indefinitely, but we believe that the factors mentioned will emphasize sufficiently the importance of high operating room standards.

Unnecessary errors or oversights may seriously interfere with the patient's well-being. These might include the following:

1. Forgetting to wear nonconductor shoes.
2. Noisy handling and dropping of instruments and pans.
3. Failure to cover the patient's eyes against the bright lights of the operating room.
4. Inadequate preparation of the operative field.
5. Carelessness in filling out the physical examination sheet, perhaps with the location of a lesion noted inaccurately.
6. The passing of an elevator while the patient is waiting on a stretcher.
7. Failure to obtain a blood grouping in the case of a seriously ill patient.
8. Improper application of a tourniquet.
9. The telling of an irrelevant story during the surgical procedure.
10. A tantrum over some trivial incident.
11. Forgetting to autoclave a routine instrument setup.
12. The use of a poor grade of materials in an attempt by hospital management to save money.
13. Inadequate lighting.
14. A leaking tube on an anesthetic machine.
15. Talking and forgetting that the patient under the drapes has been given only a local anesthetic and is therefore awake.

CONCLUSION

From the foregoing, it should be readily appreciated that every person associated in any capacity with the operating room team should take every precaution that will minimize and reduce the danger of harmful bacteria. Observance of these precautions and maintenance of only the best operating room standards will ensure the patient that he has every chance to overcome the disease or condition with which he is afflicted.

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A SURVEY OF 3,874 ROUTINE FULL-MOUTH RADIOGRAPHS

II. A Study of Impacted Teeth

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IMPACTED TEETH are a common finding among patients seen in dental practice. According to Mead,[5] an impacted tooth is one that is prevented from erupting into position because of malposition, lack of space, or other impediments. Most dentists will recommend the removal of impacted teeth if infection or pain is present, if resorption of adjacent teeth is taking place, or if there is radiographic evidence of cyst formation. This latter factor is of considerable importance, in view of the well-known propensity of ameloblastomas to develop in the walls of dentigerous cysts.[1, 6, 7] A substantial number of dentists also recommend that impacted teeth which are asymptomatic at the time of examination should be prophylactically removed to prevent complications in later years. Furthermore, it is generally agreed that if removal is anticipated at all, the surgical procedures are easier and better tolerated in younger patients.

The number of studies of the incidence of impactions has been small. In 1930 Mead[4] reported on a series of films of 6,389 cases, of which 1,462 were full-mouth radiographs of office patients and the rest were radiographs of skulls obtained from the Smithsonian Institution. Among the office patients, 276 (18.8 per cent) had at least one impacted tooth. Hellman,[3] studying a small series of university students, found the incidence of impactions to be 9.5 per cent in males and 23.8 per cent in females. In Mead's study, 461 of 581 impacted teeth (nearly 80 per cent) were third molars—248 in the mandible and 213 in the maxilla. The next most frequently impacted tooth was the maxillary cuspid, with the remainder of the impactions distributed throughout the jaws.

Although these figures are indicative of the frequency with which impactions occur in patients, they are not truly representative of the incidence of

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impactions. The latter can be derived only from comparing the number of impacted teeth with the number of normally erupted teeth found in a population sample.

The purpose of this study was to determine the incidence of impaction among various teeth, the incidence of bilateral impaction of teeth, and the incidence of radiolucent areas surrounding impacted third molars.

MATERIALS AND METHODS

A series of 2,189 full-mouth radiographs from the Indiana University School of Dentistry and 1,685 full-mouth radiographs from the Dental School of the University of Oregon provided material for this study. The 3,599 sets of radiographs from patients 20 years of age and older formed the basis of the study of impacted third molars. An additional 244 sets of radiographs from the original sample were from patients between the ages of 13 and 20. These were included in the study of impacted cuspids and other permanent teeth. The series of radiographs was selected from the files, and no radiographs were eliminated unless a set was incomplete or faulty.

In the Oregon group, the occurrence of various impacted teeth was recorded. The number of corresponding normally erupted teeth was also noted. From these data, figures on the incidence, location, bilateral occurrence within the same jaw, and age and sex of patients with impactions were derived. For the study of bilateral occurrence, only those sets of radiographs which showed both teeth in question were included. In the Indiana group, the incidence of radiolucencies surrounding the crowns of impacted third molars was recorded. For the purposes of this study, teeth which were completely impacted in bone as well as teeth which were partially in soft tissue were included since, from a clinical standpoint, all these teeth are capable of giving rise to surgical problems.

An attempt was made to record the incidence of impacted teeth which were causing resorption of adjacent erupted teeth. It was found, however, that the difficulty in interpreting mild resorption from periapical radiographs made this task impossible. The classification of radiolucencies around the crowns of impacted teeth also presented some difficulties. It was found that many impactions had a narrow zone of radiolucency around the crown which, in all probability, represented an enlarged follicular sac. The decision as to when such a space was large enough to be considered a dentigerous cyst had to be arbitrary. It may be assumed, however, that a tooth with an enlarged follicular sac has a greater potential for developing a dentigerous cyst with the passage of time. For the purposes of this study, radiolucencies were classified in two categories: (1) enlarged follicular space and (2) dentigerous cyst. The dividing line was established arbitrarily when the width of some portion of the radiolucency, particularly around the cervical third of the crown, exceeded 2 mm.

RESULTS

Of the total of 1,685 sets of radiographs from the University of Oregon, 281 (16.7) per cent showed the presence of at least one impacted tooth. The

incidence of impacted third molars is shown in Table I. It may be noted that 21.9 per cent of the maxillary and 17.5 per cent of the mandibular third molars present were impacted. This difference is statistically significant (chi square = 6.38, $p < 0.012$) and indicates that third molar impactions occur with slightly greater frequency in the maxilla than in the mandible. This finding is contrary to that reported by Mead.[4]

TABLE I. INCIDENCE OF IMPACTED THIRD MOLARS
(DATA FROM THE UNIVERSITY OF OREGON)

	TOTAL NUMBER OF THIRD MOLARS PRESENT	NUMBER OF IMPACTED THIRD MOLARS	INCIDENCE OF THIRD MOLAR IMPACTIONS (PER CENT)
Maxilla	975	213	21.9
Mandible	1,192	209	17.5*

*Chi square = 6.38, $p < 0.012$.

The incidence of impacted third molars according to sex may be seen in Table II. These figures indicate that, although a slight difference is apparent, it is not statistically significant. There were no sex differences in the incidence of impacted third molars in this study, contrary to the implication by Hellman[3] that impactions occur more frequently in girls and women.

TABLE II. INCIDENCE OF IMPACTED THIRD MOLARS ACCORDING TO SEX
(DATA FROM THE UNIVERSITY OF OREGON)

	TOTAL NUMBER OF THIRD MOLARS PRESENT		NUMBER OF IMPACTED THIRD MOLARS		INCIDENCE OF THIRD MOLAR IMPACTIONS (PER CENT)	
	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
Maxilla	441	534	86	127	19.5	23.8*
Mandible	532	660	97	112	18.2	16.9†

*Chi square = 2.67, $p > 0.05$.
†Chi square = 0.29, $p > 0.05$.

As shown in Table III, the over-all incidence of impacted maxillary cuspids was 0.92 per cent. A difference noted between the females (1.17 per cent) and the males (0.51 per cent) was at the borderline of being statistically significant at the 5 per cent confidence level (chi square = 3.81, $p < 0.053$). The remaining impacted teeth included thirteen mandibular cuspids (an incidence of 0.38 per cent), four maxillary premolars, three mandibular cuspids, and twelve supernumerary teeth.

TABLE III. INCIDENCE OF IMPACTED MAXILLARY CUSPIDS
(DATA FROM THE UNIVERSITY OF OREGON)

	TOTAL NUMBER OF CUSPIDS PRESENT	NUMBER OF IMPACTED CUSPIDS	INCIDENCE OF MAXILLARY CUSPID IMPACTIONS (PER CENT)
Males	1,167	6	0.51
Females	1,876	22	1.17*
Totals	3,043	28	0.92

*Chi square = 3.81, $p < 0.053$.

The incidence of bilateral impaction in patients in whom both teeth in question were present (both maxillary or mandibular third molars or both maxillary cuspids) may be seen in Table IV. In the case of the third molars a slightly higher number of cases of bilateral impactions was found, but the differences were not statistically significant. In the case of the maxillary cuspids, however, the greatest majority of impactions (92 per cent) were unilateral.

TABLE IV. OCCURRENCE OF BILATERAL IMPACTIONS
(DATA FROM THE UNIVERSITY OF OREGON)

IMPACTED TOOTH	NUMBER OF PERSONS WITH BOTH TEETH PRESENT	NUMBER OF CASES OF BILATERAL IMPACTION	NUMBER OF CASES OF UNILATERAL IMPACTION
Mandibular third molar	308	52	40
Maxillary third molar	388	54	50
Maxillary cuspid	1,450	2	23

Table V shows the incidence of radiolucencies surrounding the crowns of impacted third molars. It may be noted that a markedly higher number of radiolucencies occur around the crowns of impacted third molars in the mandible than in the maxilla (37 per cent versus 15 per cent). Of these, the majority (89 per cent) probably represented enlarged follicular sacs, while 11 per cent were sufficiently large to be considered dentigerous cysts.

TABLE V. INCIDENCE OF RADIOLUCENCIES SURROUNDING THE CROWNS OF IMPACTED THIRD MOLARS
(DATA FROM INDIANA UNIVERSITY)

IMPACTED TOOTH	NUMBER OF IMPACTIONS	NUMBER OF ENLARGED FOLLICULAR SPACES	NUMBER OF DENTIGEROUS CYSTS	PER CENT OF CROWNS WITH RADIOLUCENCIES
Maxillary	186	24	4	15
Mandibular	208	69	8	37

DISCUSSION

It is interesting that approximately one of every five third molars, both maxillary and mandibular, is impacted. The finding that 37 per cent of mandibular and 15 per cent of maxillary impacted third molars had some type of radiolucency around their crowns tends to support the recommendation that all impactions should be removed because of their potential to give rise to cysts and other complications.

The finding that unilateral impaction of third molars occurs almost as frequently as bilateral impaction is somewhat surprising, in view of the clinical impression of many oral surgeons and orthodontists that a strong tendency toward bilateral impaction exists. One possible explanation may be that the criteria employed in this study did not provide for recording the severity of the impaction. As a result, many unilateral impactions could have been less severe, or even partial, and perhaps would not have been considered true impactions in a clinical examination. Impacted maxillary cuspids, on the other hand, showed a definite tendency to occur unilaterally.

SUMMARY

In a comprehensive study of 3,874 routine full-mouth radiographs, the following findings concerning impacted teeth were noted:

1. The incidence of patients with at least one impacted tooth was 16.7 per cent.

2. The teeth most often impacted, in order of frequency, were the maxillary third molar, the mandibular third molar, the maxillary cuspid, and the mandibular premolars.

3. The incidence of impaction was 21.9 per cent for maxillary third molars and 17.5 per cent for mandibular third molars.

4. The incidence of impaction among maxillary cuspids was 0.92 per cent.

5. No sex differences were noted in the impaction of third molars, but maxillary cuspid impactions were found more frequently in female patients than in male patients.

6. No statistically significant predisposition toward bilateral impaction was noted among third molars, while a definite tendency toward unilateral impaction was found in maxillary cuspids.

7. Thirty-seven per cent of mandibular and 15 per cent of maxillary impacted third molars were found to have areas of radiolucency around their crowns.

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ORAL MEDICINE

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EPIDERMOLYSIS BULLOSA: A RARE DISEASE OF DENTAL INTEREST

Review of the Literature and Report of a Case

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THE purpose of this article is to discuss the clinical findings and treatment in a case of epidermolysis bullosa in which oral surgical treatment was required. Very little has been reported concerning the oral manifestations and surgical approach in this disease. Wilson[1] has reported the difficulties encountered in relation to anesthesia in epidermolysis bullosa, and a few authors have commented on the presence of deformed dental arches,[2] atrophy of the mandible,[3] and lesions of the mucous membranes of the mouth and tongue.[4]

In view of the rarity of this condition, it may be of interest to review briefly some aspects of the clinical features, etiology, pathology, and treatment of epidermolysis bullosa.

CLINICAL FEATURES

Epidermolysis bullosa is a rare hereditary disorder of the skin and/or associated structures of epidermal origin. The disease is characterized by the development of vesicles and bullae which often arise as a result of slight trauma or irritation. The bullae, however, may appear spontaneously. They contain a clear or blood-stained fluid which is initially sterile. A number of classifications have been mentioned in the literature, but the disease exists essentially in two forms—simplex and dystrophic.

Epidermolysis Bullosa Simplex.—The simplex form of the disease usually affects infants at birth or shortly thereafter. The bullae are most likely to occur at areas exposed to injury or friction, such as the tips of the fingers. The lesions usually heal and leave no scars. The mucous membranes, teeth, hair, and nails are normal. The general health is usually good, and the disease either disappears or subsides at puberty.

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Epidermolysis Bullosa Dystrophica.—The manifestations of the dystrophic type of epidermolysis bullosa are more severe. The bullae are larger and occur in mucous membranes as well as in the skin. The teeth may be absent or deficient in number. They decay more rapidly because of the patient's inability to practice good oral hygiene and because of defective enamel formation.[5] Extensive caries, periapical abscesses, jagged crowns, and retained roots may be present. The nails may be absent or show dystrophic changes. The hair may also show abnormal changes. Many of the patients are small in stature and subnormal in intelligence. On healing, the bullae leave atrophic scars, with epidermal cysts commonly present. The patients are subject to the lesions throughout life. Because of the constant loss of skin, some patients are completely incapacitated by the affliction and may not survive past childhood. The prognosis may range from chronic recurrent bullous eruptions to a fatal disorder.

ETIOLOGY

Several theories have been advanced as to the exact cause of the disease, but none of these is universally accepted. Engman and Mook[6] expressed the opinion that there is a deficiency of elastic tissue in the papillary and subpapillary layers of the skin in both the normal areas and those affected by the bullae. This deficiency is thought to account for the susceptibility of the epidermis to bulla formation following trauma.

Winer and Orman[7] have suggested that there is a primary inherited defect involving the permeability of the vessel walls. This permits transudation of serum into the upper layers of the epidermis, thus resulting in edema, bulla formation, and destruction of the elastic tissue.

A third possibility, suggested by Elliot,[8] is that of an abnormal vasomotor nerve control or cellular damage caused by a circulating toxin.

PATHOLOGY

Bulla formation and separation in the superficial layers of the skin occur in all cases. In the simplex form of the disease the bullae may involve the inner portion of the epidermis or occur beneath the epidermis. As a rule, the elastic tissue is frayed and splintered but not destroyed. In the dystrophic form of the disease the lesions are subepidermal, and considerable destruction of the elastic tissue is seen. Mild inflammatory changes may be present in the skin.[9]

DIFFERENTIAL DIAGNOSIS

In the majority of cases, according to Wilson,[1] recognition of the disease is not difficult. Wilson states, however, that it must not be confused with such conditions as dermatophytosis, pemphigus, congenital syphilis, bullous erythema multiforme, and porphyria congenita.

TREATMENT

No specific treatment for epidermolysis bullosa has been described, other than palliative therapy and treatment of secondary infection when it occurs.

Prophylaxis is therefore of the utmost importance. The rapidity with which the bullae appear and the slight trauma required for their production, in addition to the atrophic scarring seen postoperatively, present many problems for consideration.

It is readily apparent that with limited knowledge concerning the surgical management of this disease, the oral surgeon confronted with a case in which intraoral surgical procedures are required has many difficulties to overcome. An illustrative case report follows.

CASE REPORT

On Aug. 31, 1959, S. W., a 14-year-old white girl with the known diagnosis of epidermolysis bullosa dystrophica, was admitted to Children's Hospital in Louisville, Kentucky, with the chief complaint of acute oral distress.

Because of the extreme rarity of the disease and the dental profession's lack of familiarity with it, the patient was unable to obtain adequate dental treatment during her developing years. As a result, she had suffered for many years from chronic odontalgia in all quadrants which had been treated symptomatically with analgesics. The oral condition became so acute that treatment was mandatory, and the patient was admitted to the hospital for oral care.

Past History.—Initial consultation with the patient's mother revealed a most interesting history of the disease. A routine physical examination of the child at birth revealed cutaneous bullae on the inner surfaces of both legs; no other abnormalities were evident at that time. While the patient was in the nursery, however, several other similar lesions appeared, especially on areas that were in contact with bedclothes; these lesions involved the mucous membranes of the mouth, nose, and pharynx. It was believed that these areas developed secondary to trauma, as exemplified by the oral and lip lesions which appeared after the infant had nursed on a rubber nipple. Because of this condition, the infant remained in the nursery for six weeks before she was discharged with the disease unimproved and undiagnosed.

As the child developed, lesions were observed periodically in areas of trauma. When she was 3 years of age, the finger- and toenails thickened and gradually fell off. A tissue biopsy was performed, and a diagnosis of epidermolysis bullosa dystrophica was established. When the child was 6 years old, flexion contractions of the hands were noted and some of the fingers and toes had acquired webbing. The permanent teeth erupted normally but were irregularly formed. These teeth soon decayed and fractured quite easily. At this early age, dental treatment was sought, but to no avail.

During the past twelve years, the patient had been treated ineffectively with cortisone and sulfathiazole ointment. Her only relief was symptomatic. In 1951 an attempt at surgical separation of the webbed fingers and toes was unsuccessful. At the time of her admission to the hospital in 1959, the patient's therapy consisted of petrolatum gauze dressings to the bullous areas and a dietary supplement of vitamins.

The patient's oral condition had presented a problem of management since the eruption of the permanent teeth. Because of the rare nature of the disease and the misinterpretation of the physical scarring, the patient had been considered a poor risk for dental treatment. Therefore, her dental treatment had consisted only of measures aimed at symptomatic relief of pain.

The family history was noncontributory. The ancestry had been traced, and no similar illness was known. The patient had one sister, 3 years of age, in good health.

Examination.—Physical examination revealed a poorly developed, poorly nourished, cooperative 14-year-old girl of normal intelligence with generalized bullous eruptions over her entire body (Fig. 1). The lesions were particularly prominent over the elbows, hands, legs, and feet; none were present on the face. There was a flexure deformity of the hands and

feet, partial webbing of the fingers and toes, and an absence of nails (Fig. 2). Other previously involved cutaneous areas appeared atrophic and smooth, with ulceration and crust formation.

The oral examination was of particular interest. However, because of the marked scarring of the oral commissures and extensive involvement of the oral cavity with painful bullous lesions, the oral examination was limited. The buccal and labial vestibules were obliterated with scar tissue, which added further to the immobility of the lips (Fig. 3).

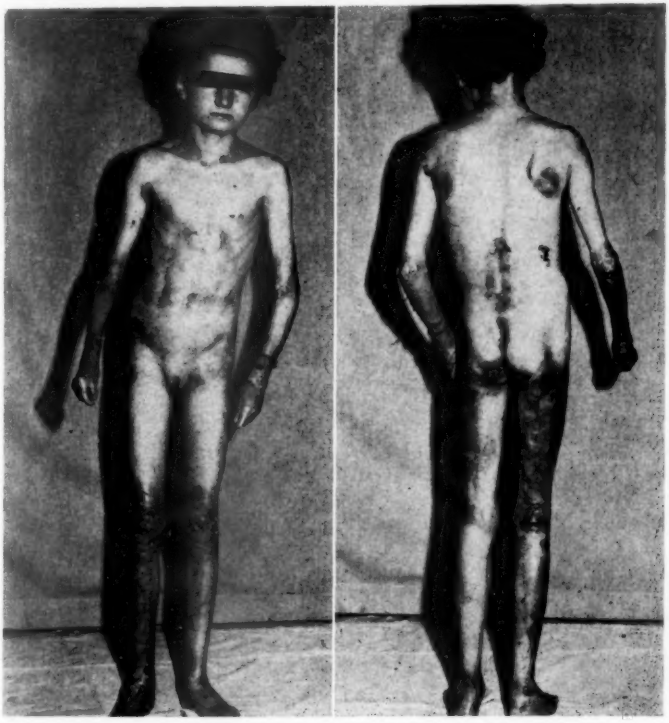

Fig. 1.—Preoperative full-body photographs taken on September 2, 1959, showing the extensive skin lesions of epidermolysis bullosa dystrophica.

Manipulation of the soft tissues with a tongue blade or retractor was impossible. Therefore, intraoral photographs and roentgenograms could not be made and lateral jaw films had to be relied upon.

The entire oral mucosa, including the lips, appeared to be extensively involved with lesions. Bullae were present in various sizes and stages; some contained fluid, some had ruptured, leaving only fragments of the oral mucosa; and others were denuded of oral mucosa, leaving a reddish, painful base. The tongue was atrophic and devoid of papillae, with generalized bullous lesions as previously described.

The teeth revealed an obvious lack of dental care. Multiple grossly carious teeth, retained roots, and jagged crowns appeared in all four quadrants. A few teeth appeared to have intact clinical crowns. The pharynx could not be visualized (Fig. 3).

Hematologic studies revealed a white blood count of 11,550, hemoglobin of 9.8 Gm. per cent, moderately hypochromic blood cells, and slight anisocytosis and poikilocytosis. Urinalysis findings were within normal limits.

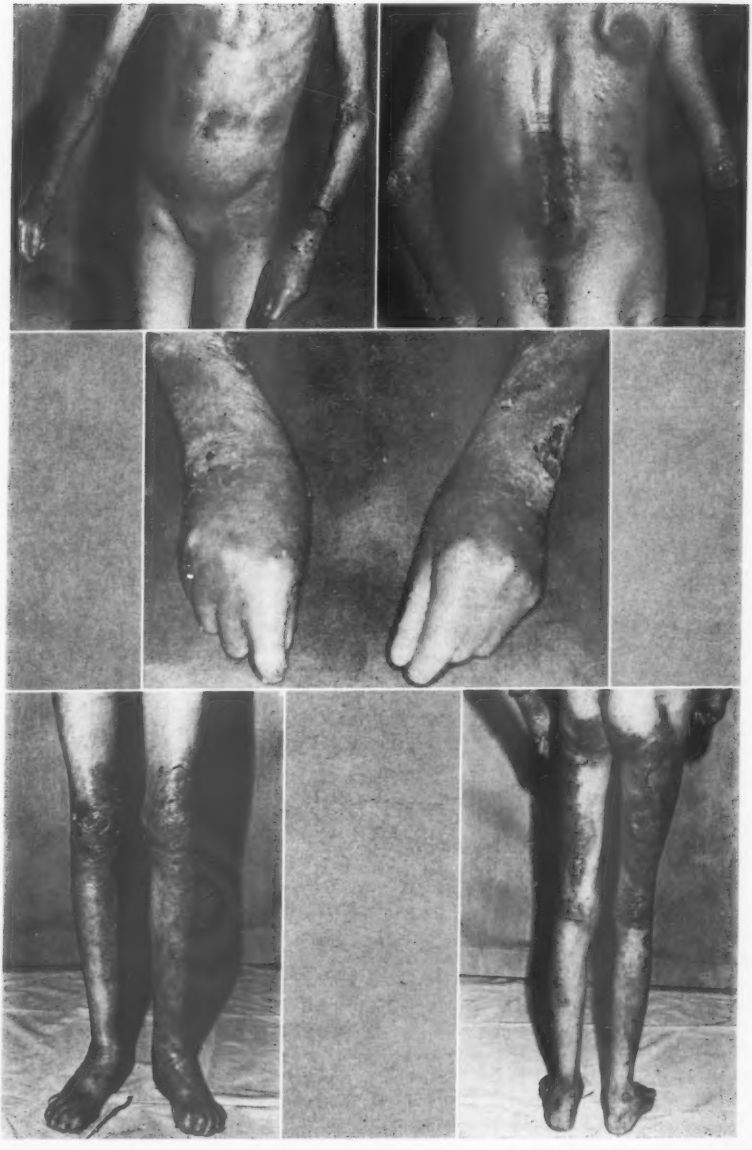

Fig. 2.—Preoperative close-up photographs taken on Sept. 2, 1959, showing generalized areas of bullous eruptions in their various stages. Note the flexure deformity of the hands, partial webbing of the fingers, and absence of nails.

Course of Therapy.—On admission, the pediatric service placed the patient on a regimen of multivitamins, wet boric-acid dressings to the affected areas, and prophylactic oral V-Cillin K tablets. Because of the low hemoglobin level, the patient's blood was typed and cross-matched, and she was given 250 c.c. of whole blood in preparation for the contemplated oral surgical procedures.

In spite of the blind surgical approach and questionable prognosis, a partial odontectomy had to be performed to alleviate the pain. It was decided to approach the problem with a conservative surgical procedure. The most accessible teeth were selected for extraction in order that the healing process might be observed. On Sept. 5, 1959, the patient was given premedication consisting of Demerol hydrochloride, 35 mg., and atropine, gr. 1/200, intramuscularly. In the operating room the mandibular incisors were anesthetized with Primacaine hydrochloride 1.5 per cent with 1:60,000 Adrenalin. These teeth were extracted atraumatically, and undue trauma to the lips was carefully avoided. The patient was most cooperative and tolerated the procedure well.

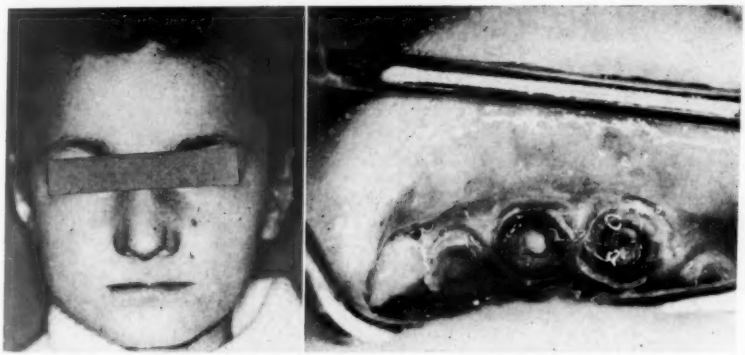

Fig. 3.—Preoperative facial photographs taken on Sept. 2, 1959. The intraoral photograph was taken with extreme difficulty, because of the painful bullous involvement of the mucous membranes. The mucobuccal fold is completely obliterated as a result of marked scarring secondary to the healing process of the lesions. Advanced dental caries is obvious in the anterior teeth.

The healing process was observed for ten days. During this time there appeared to be adequate granulation and closure of the sockets, with no secondary infection or hemorrhage. However, the patient still complained of odontalgia in the posterior teeth.

In view of the satisfactory response to the initial operation, it was decided that the remaining diseased teeth should be removed. Because of the contracted scarring of the lips and the limited size of the oral opening, a general anesthetic was indicated.

On Sept. 17, 1959, the patient was premedicated and taken to the operating room. A nasal endotracheal tube was inserted, and anesthesia was induced with nitrous oxide-oxygen and Flouthane. The patient was draped in the routine manner. The operation proceeded with difficulty, because of inadequate exposure. Retraction of the lips and cheeks resulted in an immediate "peeling" of the superficial mucosa. The remaining carious teeth and retained roots were removed with a minimal amount of surgical manipulation. Clinically sound teeth were retained for use in mastication. The tissue was extremely friable, and no attempt was made at suturing. Hemostasis was accomplished with gauze packs, and the patient was returned to the recovery room awake.

The patient responded well postoperatively; the effects of surgical trauma, although extremely minimal, were obvious. The immediate postoperative course was satisfactory, and the patient was ambulatory on the first postoperative day.

On the second postoperative day, multiple bullae appeared as a result of the surgical trauma and manipulation. The largest and most obvious lesion, measuring 4 by 3 cm., was

present on the lower right lip. This lesion, which appeared similar to the skin lesions on other areas of the body, was attributed to the manipulation by the surgeon from the right side of the operating table (Fig. 4).

The patient was observed postoperatively for five days. During this time the healing process was satisfactory. No evidence of infection or hemorrhage was seen. Although the mucous membrane lesions were uncomfortable, the excruciating pains of generalized odontalgia were alleviated.

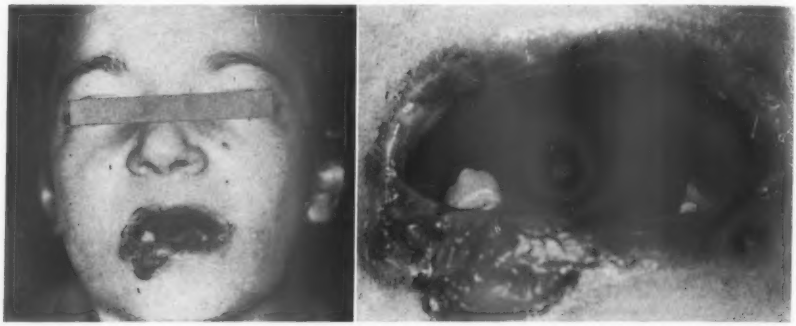

Fig. 4.—Photographs taken on Sept. 18, 1959, twenty-four hours postoperatively. As compared to the preoperative views, the extensive formation of bullae is readily evident. These bullae are attributed to surgical trauma in spite of the delicate manipulation of the tissues.

Fig. 5.—Follow-up photographs taken on Feb. 6, 1960 (five months postoperatively) showing absence of the mucous membrane lesions that were attributed to surgical trauma. However, the scarring of the oral commissures is still present and perhaps accentuated. Loss of flexibility is evidenced by microstomia, and the tongue remains devoid of papillae.

The patient was discharged on Sept. 22, 1959, to be followed in the outpatient clinic. Unfortunately, because of the inconvenient distance involved, she was unable to return to the clinic and was followed by her family physician.

The patient was seen again on Feb. 6, 1960, five months after the surgical procedures. At this time the oral condition was remarkably improved, and the acute oral distress had been relieved. There were no obvious lesions on the mucous membrane, and the oral mucosa was of a good color. Scarring of the oral commissures was still present, however, and was perhaps accentuated. The oral examination was still limited, and manipulation of the tissues caused discomfort (Fig. 5).

DISCUSSION

The foregoing case was presented because of its unusual and rare nature. A review of the literature yielded little information regarding the care and management of such lesions of the oral cavity. In spite of the generalized nature of the disease, the patient was admitted to the hospital for alleviation of acute oral distress.

This patient obviously suffered the discomforts of extreme dental neglect. Because of the chronic systemic manifestations of her disease, she had been considered a poor dental risk and had been unable to receive treatment. Only when the oral condition became so acute that treatment was mandatory was the patient admitted to the hospital for dental care. Tooth extractions via a conservative surgical approach alleviated the patient's distress. Careful surgical manipulation minimized the severity of the bullous lesions that developed postoperatively.

COMMENTS

1. We are not prepared to attribute the initial oral lesions in the case just described entirely to epidermolysis bullosa. Much consideration must therefore be given to the secondary infection associated with dental neglect. It has been our experience, however, that bullous lesions developed quite readily in normal areas when subjected to trauma.

2. We were quite concerned with the healing process associated with this disease. Again, it has been our experience that healing of the alveolar sockets was uneventful.

SUMMARY

The clinical features, etiology, pathology, and treatment of epidermolysis bullosa have been briefly reviewed. A case in which oral surgical treatment was required has been presented, and the clinical course has been discussed in detail.

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ORAL ROENTGENOLOGY

American Academy of Oral Roentgenology

Arthur H. Wuehrmann, Editor

PANAGRAPHY

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THE introduction of panoral radiography to the science of dentistry may well stimulate a broader outlook and approach to the x-ray examination of the teeth. The techniques of intra- and extraoral radiography are segmental or sectional in practice, and both are prone to produce distorted pictures with superimposed shadows. Neither can be claimed to be so standardized in execution that it can be repeated under exactly the same conditions for comparative purposes in the control of treatment.

Every technical advancement in dental radiography is aimed at overcoming these drawbacks, improving the output of the apparatus, employing more rapid films, reducing exposure time, simplifying the operation, and, above all, protecting the patient and the operator against possible radiation hazards.

With the sharp and distinct division between coronal affections, marginal periodontitis, and periapical disease, radiography of the teeth has resolved itself into bitewing and periapical techniques. The patient is thus likely to be submitted to a twofold x-ray examination with attendant increasing radiation risks.

Panoral radiography is able to produce a single-plane panoramic picture of each arch. The same film shows the supporting structures of the teeth in good detail and with fine contrast. The size of the teeth is automatically magnified to about twice the normal anatomic length. This permits complete depiction of the crown, the alveolar margin, the full length of the root, the surrounding supporting bone structures, and a more extensive amount of osseous structure beyond the tooth apex. All of this can be done without superimposed shadows. This form of x-ray examination can be standardized for reliable repetitive pictures. It is free from objectionable penumbra and has only a minimal amount of distortion.

*Director, Department of Radiology.

The source of radiation is placed within the oral cavity. Radiation emanates from a target anode set at the distal end of a long projection from the main glass x-ray bulb. This tube extension is introduced into the mouth.

The conception of an intraoral source of radiation is by no means new. In 1897 Rollins, in the United States, and Bouchacourt, in France, simultaneously conceived the idea of introducing a small x-ray tube into the oral cavity and projecting the images of the teeth onto a film placed outside the face. Those were the days of the bulky gas tubes with focal targets too large to produce sharp pictures. Very little progress was made in this direction until just after World War II, when the discovery of a large range of radioactive isotopes stimulated Mayneord in England to pronounce that "The discovery of a large range of radioactive isotopes made it probable that by suitable choice of substances available in sufficient quantity, they might, in some instances, even displace x-ray tubes or, much more probably, enable radiographs of the human body to be taken under entirely different circumstances." The results obtained with the radioactive isotopes were most revealing, but isotopes are costly, their lives are relatively short, and the radiation risks are forbidding.

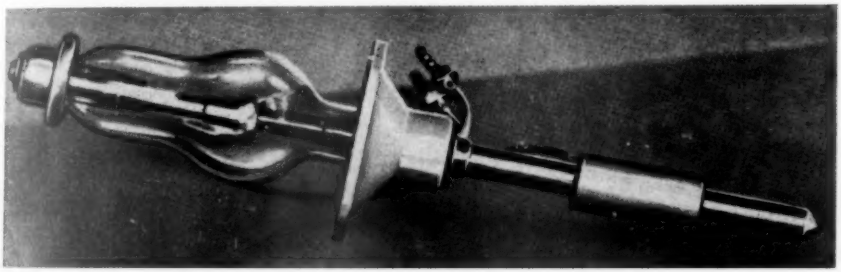

Fig. 1.—Long-rod anode x-ray tube used in industry for the examination of tubular constructions.

About 1938, industry was using a special x-ray tube (Fig. 1) for the examination of such tubular constructions as the pipes of a steam boiler or the cylinder bores of an internal-combustion engine. These x-ray tubes were constructed with an extending arm from the center of an x-ray bulb and the anode target was placed remotely at the free end of the extension. These were known as long-rod anode radiographic tubes and were soon followed by the Chaoul radiotherapy tubes; the latter were of a similar design but were employed for rectal and vaginal irradiation.

THE X-RAY TUBE

The x-ray tube used in the Panagraph is the Swiss Panoramix tube (Fig. 2). It is similar to the Chaoul therapy tube, but it has an extremely fine focal area and gives a 270 degree angle of radiation divergence in two perpendicular planes.

The cathode is centrally placed in the Panoramix tube and is composed of solid tungsten in the shape of a long cylinder. It is heated by indirect means

with an electron bombardment to produce a homogenized electron beam. A special automatic device is embodied in the tube to center the cathode stream on the focal spot.

The anode target is a small copper cone with a tungsten apex; its base is set at the distal end of the long glass hollow arm. The tip of the cone is reduced to the size of a pin point, so that the actual focal area is an ultrafine spot of only $\frac{1}{250}$ inch. It is directed along the true axis of the tube extension in line with and pointing backward to the center of the cathode. When activated, the x-rays emanate from the point focus which is inside the oral cavity and diverge toward the teeth with a wide-angle divergence. In this way, they project the images of the teeth onto a film held on the outside of the face.

The film-focus distance is extremely short (about 4 cm.), but the point focus compensates for the short distance and is responsible for the sharpness of detail. The short film-focus distance, together with the wide divergence of

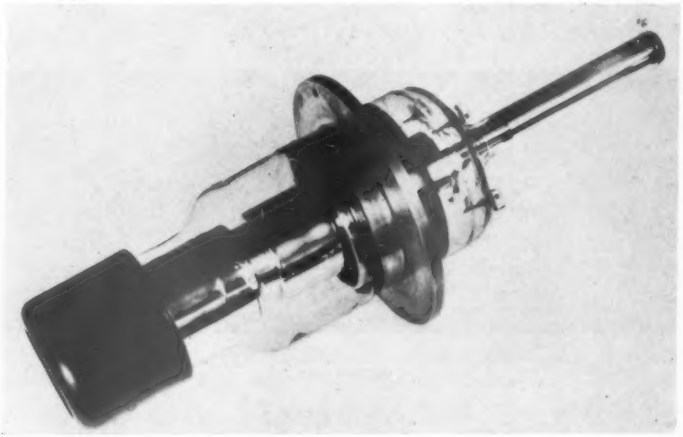

Fig. 2.—The Panoramix x-ray tube, with long glass hollow projection carrying the target anode at its distal end.

the x-ray beam, produces a magnification of the image which is at least twice the normal anatomic size. The more closely the film is adjusted to the face, the less is the degree of magnification. The target is electrically connected by a thin metal sheath to the oil-immersed parts within the tube, and the arm is covered with lead foil to prevent the spread of divergent radiation to the base of the skull. The anode target and metal sheath are grounded. The tube insert is housed completely in a metal protective case; there should be no leakage from this housing. The rating of the x-ray tube is low; the tube is immersed in oil; the anode is cooled by convection. Under such circumstances, no special cooling system is necessary. With an exposure time of 0.1 second at 0.5 Ma. and an activating potential of 60 kv., the thermal capacity of the shield and anode permits one exposure per second.

THE CONSTANT-POTENTIAL GENERATOR

The Panoramix x-ray tube cannot be operated with a normal transformer. Modern x-ray diagnostic apparatus demands a *high-energy* electrical supply to activate the x-ray tube for *short periods*. For radiotherapy, constant-potential generators are often employed in which condensers are used to smooth out pulsations of ordinary rectified alternating current.

This is the type of generator which is used with the Panoramix tube. The radiation resulting from the application of a constant potential to the tube has a greater number of highly penetrating photons than that produced by a pulsating current having the same peak voltage. In the latter case the majority of the electrons in the cathodal stream differ in peak energy. The elimination of this difference leads to a greater intensity of useful x-rays with less heating of the target. Thus, no special cooling device is necessary for the anode.

Fig. 3.—The Panagraph, a compact, mobile, transportable apparatus.

The generator tank contains at high potential an electronic stabilizing circuit which maintains the temperature of the cathode at a very constant level under all conditions. Therefore, a constant and stable tube current is maintained. The electron beam is permitted to pass through to the anode by an auxiliary electrode in the cathode assembly which operates in the manner of a control grid in an electronic valve. The voltages necessary to prevent the beam from passing, or to permit it to pass to the anode, are also generated in this circuit at high potential. The exposure time is that for which the permissive voltage is applied. This constant-potential generator is capable of producing a kilovoltage of between 50 and 70.

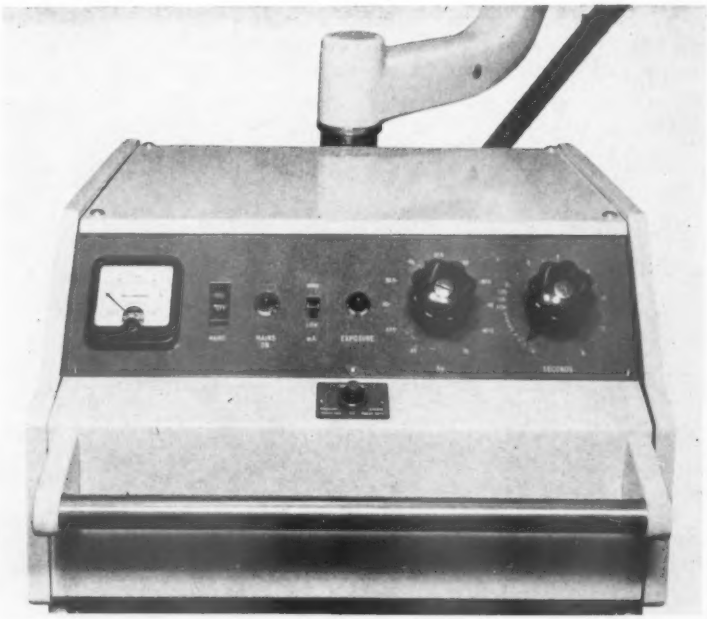

Fig. 4.—Control panel of the Panagraph.

When activated by a difference in charge between the anode and the cathode, the cathodal stream is propelled as a narrow beam of small diameter in the true horizontal axis toward the remote target anode at the distal end of the projection. In the anode extension the electron stream is easily deflected by a magnetic field, and the control of this stream requires a very special centering device. Centering electromagnets are built in the tube itself, and the currents passing through these magnet coils are controlled through an electronic amplifier unit which is contained in the control stand of the generator. This automatically produces a deflection of the electron stream in order to correct a possible deviation caused by an external factor.

These important controls concentrate the electron beam permanently upon the pin-point target, restrict any straying of the stream, and obviate the possibility of puncturing the glass extension.

The Panagraph is an Anglo-Swiss development (Fig. 3), compact and mobile. It uses the specialized Panoramix x-ray tube. It is constructed as a transportable apparatus, mounted on wheels and adapted so that it can be taken to any clinic, school, or establishment where mass dental radiography is contemplated. The main components of the Panagraph are an enameled metal cabinet containing the high-voltage generator, an arm bracket, the Panoramix tubes, cables, and a synchronous timer. The controls are grouped on an upper panel (Fig. 4) which includes a milliampere or milliampere-seconds meter (to read the current passing through the tube) and an adjustable synchronous timer. This latter instrument is an important adjunct, as the exposure times are as low as one-tenth of a second. The apparatus can be operated from any well-grounded household electrical outlet capable of providing 110 to 240 volts.

Every effort is made during the panoral examination to restrict the exposure time. It is recommended that only high-speed films be used and that these be enclosed in special plastic cassettes which are lined with a calcium tungstate layer to enable them to act as intensifying screens. The cassettes may be lead-backed so that the patient can hold them in position without receiving any radiation to the hands.

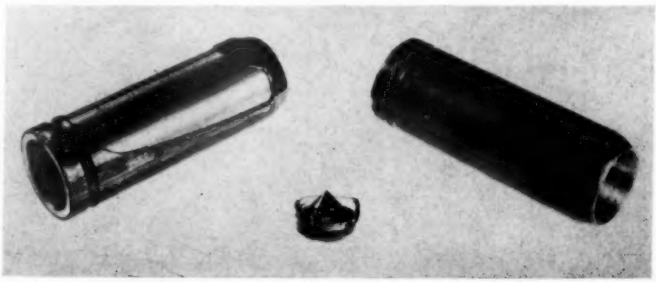

Fig. 5.—Cylindrical applicators made of aluminum and lead which are drawn over the tube extension as additional filters and to define the beam. The conical anode is also shown (center).

THE PANORAL TECHNIQUE

1. The patient is seated upright in a chair, preferably with a head support.

2. The head is adjusted so that the sagittal plane is vertical. It may be maintained in position by a light metal craniostat connected to the tube head.

3. The upper and lower occlusal planes are used to set the head for maxillary and mandibular teeth, respectively. The appropriate occlusal plane should be parallel to the floor.

4. Special applicators of aluminum and lead are drawn over the tube extension for additional filtration and for restriction of the beam to the correct

angle (Fig. 5). There are special applicators for the upper and lower jaws. These have diameters of just under 1 inch for adult patients and ¾ inch for children.

5. The applicators can be sterilized or covered with polythene sheaths that are freshly cleaned for each patient.

6. The tube head, carried on the arm bracket of the apparatus, is lowered to the level of the patient's mouth, and the patient is encouraged to receive the tube extension.

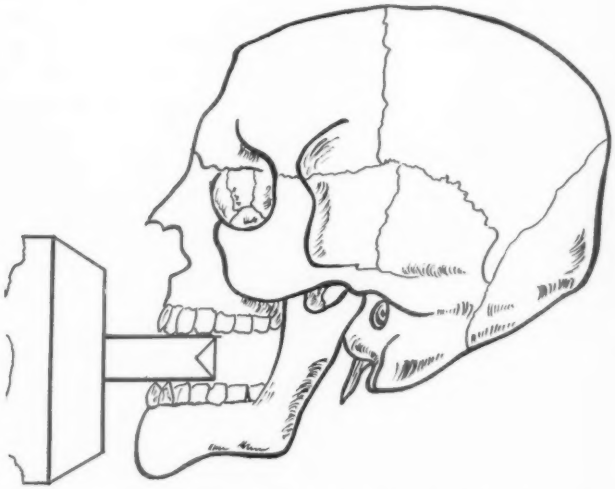

Fig. 6.—Diagram showing the tube extension introduced to the transverse axis of the second permanent premolars.

7. The further the extension is introduced into the mouth (Fig. 6), the larger will be the panoramic picture of the arch. There is no necessity for the anode target to be placed more than 3.5 cm. in the oral cavity. The tube extension is calibrated to show the extent of its introduction into the mouth.

8. The patient is enjoined to bite on the applicator, preferably on a cotton-wool roll, to elevate the incisive margins of the teeth.

9. The tube head is adjusted to an angle upwards of 30 degrees (Fig. 7) for the upper jaw, and to an angle downwards of 20 degrees for the lower jaw. These angles serve to locate the focal spot adequately within the particular arch in order to project the images of the teeth on the film in correct relationship. The angles are controlled by a special angulometer carried on the tube head.

10. The 10 by 3 inch film in a plastic cassette is placed against the outer side of the face; one film is used for the upper jaw and another is used for the lower jaw, in sequence. The cassette can be held by the patient or maintained by a nylon band attached to the head support.

11. The lower edge of the cassette is directed upward for the upper jaw and downward for the lower jaw in order to ensure that the images of the teeth are

recorded substantially parallel to the edge of the film. This is necessary because it is not possible to position the focal spot high enough or low enough in the mouth to be in the same plane as the arch itself. The cassette should be molded in close proximity to the face.

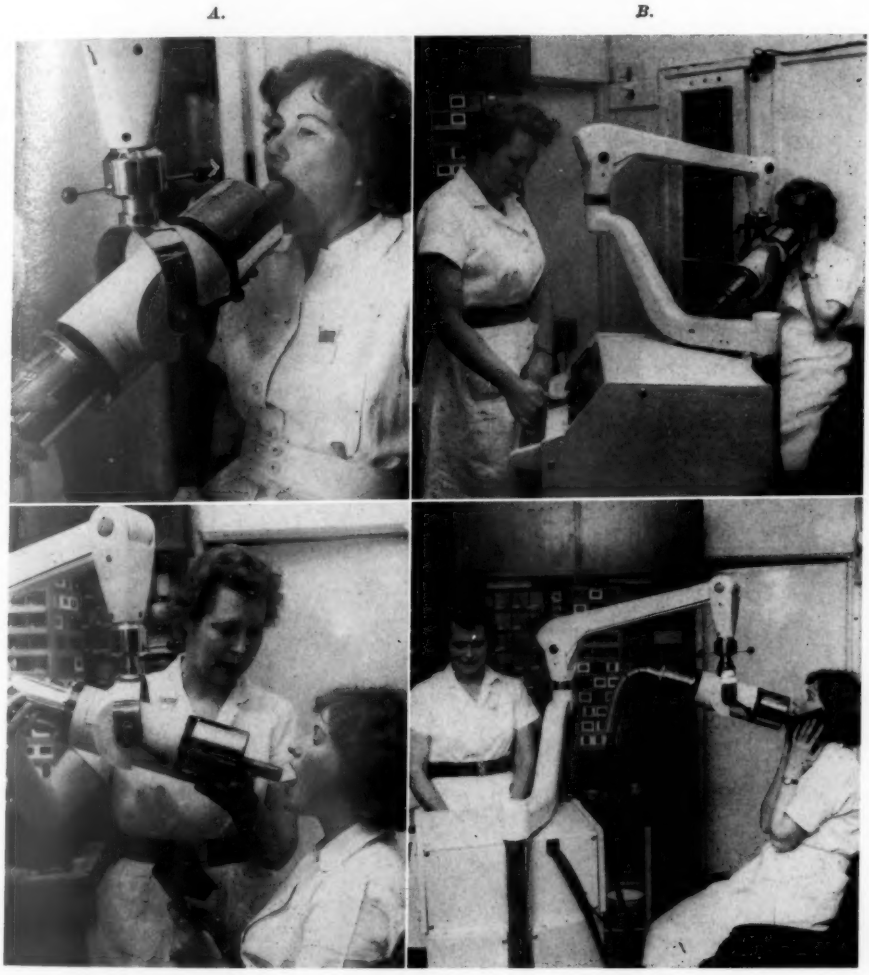

Fig. 7.—*A* and *B*, Technique for the maxillary teeth, showing upward inclination of the tube head.

C and *D*, Technique for the mandibular teeth showing downward inclination of the tube head.

12. For adults, a current of 0.5 Ma. is passed through the tube at an applied voltage of 60 kv. An exposure time of 0.1 second is ordinarily used.

If a wider film is used for the upper jaw with an applicator permitting a wider angle of radiation, a good view of the maxilla and antrum is obtainable. Lower occlusal views may be obtained as illustrated in Fig. 8.

Fig. 8.—Technique for lower occlusal radiography.

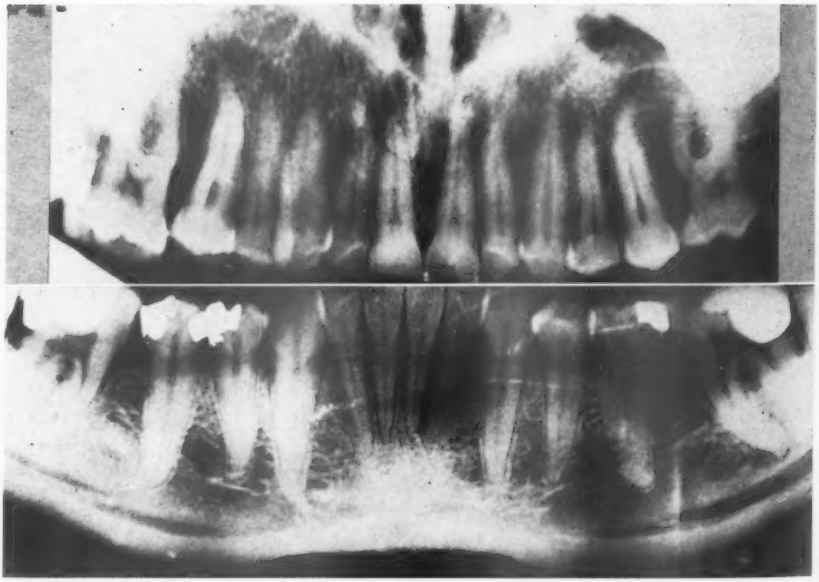

Fig. 9.—Panoral radiographs of the upper and lower jaws.

Restricted introduction of the target anode will produce a greater magnification of the incisors, better isolation of the crowns of the premolars, and limited panorama. The further the target anode is introduced into the mouth, the wider the panorama and the greater the overlapping of the crowns of the premolars (Fig. 9).

RADIATION DOSAGE IN PANORAL RADIOGRAPHY

Radiation measurements have been made both at the Royal Dental Hospital in London and also in Berne, Switzerland, in an attempt to assess the dosage to the patient during panoral radiography.

The dose rate delivered by the unit depends critically upon distance and direction from the focus of the x-ray tube. An average dose, in air, at a distance of 5 cm. from the focus, with 2.5 mm. aluminum added filter and exposure conditions of 60 kv., 0.5 Ma. and 0.1 second, is approximately thirty-three mr. These exposure conditions are typical of those used in practice.

Because of the very short focus-tissue distances involved here, the actual dose received by the inner surface of the epithelial tissue within the mouth will vary over wide limits. The tongue is nearest to the tube focus, since the tube projection rests directly against it during exposure. There is no need for the tongue to be exposed to direct radiation, however, as it can be shielded by lead embodied in the applicators. This lead shielding defines a field of approximately the area of the film (21 cm. wide by 7.5 cm. high) when it is bent around the face forming, roughly, part of a cylinder with a radius of 5 cm.

To obtain an estimate of tissue and skin dose from the "in air" output quoted above, estimates have to be made of the focus-tissue distances actually encountered, the effective field size at this tissue surface, and the thickness of tissue involved. Two cases have been chosen for calculation—one in which the inner surface of epithelial tissue within the mouth is 2 cm. from the tube focus and a second in which this distance is 3 cm. The skin is assumed to be 5 cm.

TABLE I

	PANAGRAPHY SINGLE EXPOSURE		NORMAL INTRA-ORAL TECHNIQUE SINGLE EXPOSURE	
	CASE 1	CASE 2	CASE 1	CASE 2
Focus-inner epithelial tissue distance	2 cm.	3 cm.	23 cm.	22 cm.
Tissue thickness	3 cm.	2 cm.	3 cm.	2 cm.
Focus-skin distance	5 cm.	5 cm.	20 cm.	20 cm.
Effective field size at skin	21 by 7.5 cm.	21 by 7.5 cm.	8 cm. circle	8 cm. circle
Tube potential	60 kv.		60 kv.	
Exposure time	0.1 second		0.5 second	
Tube current	0.5 Ma.		10 Ma.	
Added filter	2.5 mm. aluminum		2 mm. aluminum	
Film or film-screen combination	Fast screens and film		Fast non-screen film	
Dose to inner epithelial tissue	240 mr.	110 mr.	110 mr.	160 mr.
Dose to skin	18 mr.	23 mr.	310 mr.	310 mr.

from the focus in both cases, thus giving tissue thickness of 3 cm. and 2 cm., respectively, and corresponding effective field sizes of 8.5 by 3 cm. and 12.5 by 4.5 cm. These conditions and the doses received by the tissue and skin are summarized in Table I. For the purpose of comparison, conditions and doses are included for a single exposure by the normal intraoral technique.

As shown by the table, the dose to the inner surface of the epithelial tissue is of the same order for each technique. There is, however, considerable variation in the dose from the panoral unit. Exposure for exposure, the skin dose from the panoral unit is approximately fifteen times smaller than the dose from a single exposure of the normal technique. It should be remembered, however, that sometimes up to seven exposures are necessary for the normal intraoral examination to give as much information as provided by a single panoral exposure. Thus, the total absorbed energy to the irradiated body tissues from one panoral exposure will be less than one-half that from a single normal intraoral exposure and only one-fifteenth that of a series of seven normal intraoral exposures. From a panoral exposure the maximum inner epithelial dose, even under the most adverse conditions, is unlikely to exceed 0.5 r, while the skin dose will be of the order of one-tenth of this.

Because of the short focus-tissue distances used in panoral radiography, the dose fall-off is very fast; thus, a minimum unnecessary exposure is given to such regions as the brain, spine, and lymphatic tissue. In fact, the "direct" beam is always directed out of the body to the film; all the rest of the body is shielded by the lead of the applicators. This also implies that the gonadal dose will be completely negligible for panoral radiography.

SUMMARY

The potentialities of this new technique in dental radiography are apparent to all those interested in the dental welfare of the population, especially of the child and adolescent. During the years when the second dentition permanently replaces the temporary deciduous dentition, it is important to observe, control, and, if possible, adjust the eruption of teeth. The latter are essential for the true growth and configuration of the face, for mastication, and for speech. It is in these years that techniques of dental radiography may prove difficult to practice and are most resented by the young patient.

The panoral technique gives us a quick and facile procedure for large-scale surveys of the teeth which will permit early and accurate identification of dental aberrations and disease. Maany of the diseases and deformities which are found in the mouth and jaws of the adult might well have been prevented or adjusted if they had been recognized in early life.

The Panagraph is easy to operate, simple to adjust, and consistent in results. The patient is readily immobilized in a stable position; the intraoral dental films are replaced by one single extraoral film for each jaw; the shortest possible exposure time is employed; and, while achieving a full panoramic view of the jaws and teeth, radiation risks are greatly reduced.

Experiments are in progress to determine the practicability of using the Panagraph for regions outside the mouth. Already promising results are seen in the field of maxillofacial work in otorhinology, and it would seem advantageous to investigate areas which are accessible through either natural or artificial openings.

I am most indebted to B. J. Perry, PH.D., B.Sc., A.R.C.S., Physicist to St. George's Hospital, London, for the careful measurements undertaken in connection with the Panagraph at the Royal Dental Hospital.

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ROENTGENO-QUESTIONS

What additional diagnostic aids, other than x-ray films, are needed in distinguishing a granuloma from an early-stage cementoma?

A granuloma at the apex of a tooth is one of several reactions which may follow the death of the pulp. An early-stage cementoma is a tumor which often occurs at the apex of a tooth. The cells of this tumor apparently originate from those whose function it is to maintain the integrity of the cementum. This interesting tumor cannot be differentiated in its early phase from a benign periapical fibroma. The cells in the latter apparently arise from those in the periodontal membrane. In the later stages of these tumors, the cells revert to their former function of laying down either cementum or bone, as the case may be. In the former tumor, this may be observed at the apices of teeth as an amorphous-appearing material. It is usually separated from the surrounding bone and the apex of a tooth by a roentgenolucent line. In the case of the benign periapical fibroma, the new bone which is laid down cannot be differentiated from the original bone which was replaced by the tumor.

Since the vitality of the tooth determines the presence of a granuloma or any of the other reactions following the death of the pulp, the use of thermal agents, such as hot gutta-percha or ice, applied to the crown of the tooth is most helpful. If the pulp is dead and a rarefaction is present, the reaction to heat or cold will be negative. In the case of the early phase of the cementoma or benign periapical fibroma, a positive response will be obtained.

The American Academy of Oral Roentgenology solicits from the readers of ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY any questions which deal with technical or interpretive aspects of oral roentgenology. These questions should be sent directly to the editor of this section, Dr. Arthur H. Wuehrmann, School of Dentistry, University of Alabama Medical Center, Birmingham, Alabama; the editor will distribute them for reply to a suitable group within the Academy. Questions, with the answers, will be published at as early a date as possible in "Roentgeno-Questions." Questions, especially those of an interpretive nature, should ordinarily be accompanied by good-quality roentgenograms and a pertinent history. The names of the questioner and the respondent will not be published.

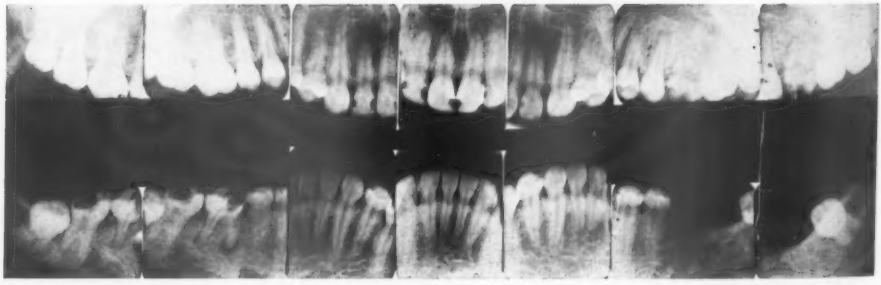
ROENTGENO-ODDITIES

Sickle-Cell Anemia

THE accompanying roentgenograms, consisting of a lateral skull projection, a posteroanterior skull projection, and a complete mouth survey, demonstrate some of the initial osseous signs of sickle-cell anemia. The radiologist reporting on the extraoral films was not prepared to go beyond a statement to the effect that the granularity in the skull bones and in the facial bones was

Each month this section will bring to the readers of ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY one or more roentgenograms which demonstrate unusual, unexpected, rare, or bizarre roentgenographic changes. These roentgenograms will be accompanied by an explanation or by words of inquiry regarding the particular change. All films used in this section will be accepted with the understanding that 2 by 2 or 3¼ by 4 inch slides or glossy photographs of the films will be made available to interested readers through the editor of the American Academy of Oral Roentgenology at the individual's expense. The cost will involve only the photographer's charges. Each slide or print will give credit to the donor. Interesting roentgenograms are solicited from all sources. Please be certain to identify your films properly so that they can be returned. All material for publication should be submitted to Dr. Arthur H. Wuehrmann, University of Alabama School of Dentistry, Medical Center, Birmingham, Alabama.

compatible with bone marrow hyperplasia. He did not believe that it was marked enough to be definitely diagnostic of this. The intraoral films suggest signs of



osteoporosis, although there is evidence of condensing osteitis in areas of probable chronic apical disease. These roentgenographic signs cannot be considered pathognomonic of the disease in question.

The roentgenograms are those of a 28-year-old Negro woman who presented with acute abdominal pain on May 6, 1961. Blood studies showed that she had a true sickle-cell anemia, type ss. During the course of therapy, the lower right first and second molars and the upper left first molar were extracted. Prior to treatment the patient received 500 c.c. of fresh whole blood. Her hemoglobin level rose from 5.6 to 8.2 grams as a result of the transfusion. The oral surgical procedure was performed without complications; the postoperative healing was uneventful.

Contributor's name withheld by request.

ORAL PATHOLOGY

American Academy of Oral Pathology

Donald Kerr, Editor

INTRAORAL MINOR SALIVARY GLAND TUMORS

An Analysis of 1,414 Cases

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PURPOSE OF THE STUDY

A CONSIDERABLE body of literature has been written on classification, clinical behavior, histogenesis, histopathology, treatment, and prognosis of tumors arising from the major salivary glands, but few well-documented reports have appeared on neoplasms of intraoral minor salivary gland origin.[20, 23, 25, 57, 63, 78, 103, 115, 151] This is largely due to the fact that such tumors are relatively far less common. According to Willis,[160] for every 100 parotid tumors, there are likely to be ten submaxillary gland tumors, ten tumors of minor salivary glands, and one sublingual tumor. Thus, not enough cases have been available in the collection of a single investigator to warrant a reliable analysis of their various features. This would also explain why the literature in the past has been based chiefly on a small series of cases or even single case reports. This lack of an adequate number of cases has resulted in disparate findings in the series of different investigators. For example, there appears to be a lack of unanimity even on such a basic question as whether benign or malignant tumors occur more frequently in the minor oral salivary glands.[25, 63, 103, 115] Similarly, conflicting reports have appeared concerning the most common histopathologic variety of tumors arising from such glands.[20, 25, 63, 103]

Another variable which could have partly accounted for such difference of opinions might have been the source from which an investigator had drawn

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his material for analysis. It is to be expected that there would be a greater number of malignant tumors in a series collected from a large hospital equipped for major surgical opoerations, radiation, and chemotherapy. On the other hand, benign tumors are frequently treated in private offices or small hospitals. Thus, it is quite possible that in some instances findings might have been based on a biased sample. Furthermore, information concerning the final outcome of treatment of such neoplasms has often been unsatisfactory. Therefore, a prognosis similar to that of the histologically identical neoplasms of the major salivary glands has been given, not infrequently, to tumors of minor salivary gland origin. However, because of differences in anatomic location, environment, and management, this may not be justified.

The present study was undertaken with the following objectives in mind: (1) to collect all available cases from the files of several Twin Cities hospitals and pathology laboratories and to analyze such aspects as their clinical behavior, histopathologic characteristics, and prognosis; (2) to ensure a large sample size for a statistically significant analysis of different features of such tumors by collecting the findings from cases reported in the English-language literature from 1927 to 1960; (3) to compare and contrast, when possible, the findings of such tumors with those arising from the major salivary glands.

MATERIALS AND METHODS

The material consisted of ninety-four cases of intraoral minor salivary gland tumors collected from the files of various Twin Cities hospitals, both large and small, as well as from the pathology laboratories of the Schools of Dentistry and Medicine, University of Minnesota, from 1939 to 1960. This helped to ensure a random sample. The medical record of each patient was reviewed, and the microscopic sections of the tumors were re-examined; when necessary, paraffin blocks of the tumors were obtained, fresh sections were cut, and special stains were employed. In order to obtain information on the latest medical status of the patients, letters were written to the physicians, dentists, or families of the patients.

The English-language literature from 1927 to 1960 (both years inclusive) yielded 1,320 cases of intraoral minor salivary gland tumors. Tumors originating in the paranasal sinuses or in the tonsillar region were excluded from this survey. There were few instances in which the site of origin of the tumor was difficult to ascertain because of extension into the surrounding structures. Cases reported by Ahlbom[2] and Hoboek[83] were not included, since their classification of salivary gland tumors into such varieties as "semimalignant" or of "questionable malignancy" was to hard to interpret objectively and, therefore, could not be adapted to our system of classification. In order to determine the relative frequency with which different histopathologic types of minor salivary gland tumors occur, we had to assume that the number of cases reported in the literature represented the relative frequency with which such tumors would occur in any given large series.

RESULTS

Among ninety-four intraoral minor salivary gland tumors, forty-three (46 per cent) were benign and fifty-one (54 per cent) were malignant neoplasms. Benign tumors included forty pleomorphic adenomas and three papillary cystadenomas. The malignant group was composed of nineteen cylindromatous adenocarcinomas, seventeen adenocarcinomas (including four papillary types, one mucus-producing adenocarcinoma, and one of the trabecular variety), ten mucoepidermoid tumors, three malignant pleomorphic adenomas, one undifferentiated carcinoma, and one unclassified carcinoma (Table I).

TABLE I. CLASSIFICATION, SEX, AND AGE DISTRIBUTION

TUMOR TYPE	NO.	PER CENT	SEX			AVERAGE AGE (YEARS)
			MALE	FEMALE	NS*	
I. Benign						
Pleomorphic adenoma	40	43	15	21	4	46.2
Papillary cystadenoma	3	3	1	2	0	40.0†
Total	43	46	16	23	4	45.8
II. Malignant						
Pleomorphic adenoma	3	3	1	1	1	64.3†
Adenocarcinoma	17	18	12	4	1	61.5
Cylindromatous adenocarcinoma	19	20	10	8	1	57.5
Mucoepidermoid (low-grade)	7	8	3	4	0	45.0
Mucoepidermoid (high-grade)	3	3	2	1	0	63.6†
Undifferentiated carcinoma	1	1	1	0	0	83.0†
Unclassified carcinoma	1	1	1	0	0	42.0†
Total	51	54	30	18	3	58.6
Total cases	94	100	46	41	7	53.0

*Not specified.
†Not statistically significant.

In the eighty-seven cases in which the sex of the patients was specified, tumors occurred in forty-six men and forty-one women. Benign tumors were slightly more common in women, and malignant tumors occurred a little more often in men. A preponderance of adenocarcinoma in men appeared significant. Age was specified in eighty-four cases and ranged from 15 to 92 years, the average being 53 years. Benign tumors occurred with almost equal frequency from the second to the ninth decades except for the third decade, in which there was an incidence of 33 per cent. Malignant tumors occurred more frequently from the fifth to ninth decades, the highest incidence being in the sixth decade. The average age of patients with benign tumors was 45.8 years, compared with 58.6 years for those with malignant neoplasms. Location was listed in eighty-eight cases, and 60 per cent of both benign and malignant tumors occurred in the palate (Table II). Duration of the lesions prior to diagnosis was mentioned in only fifty-two cases. While the median duration in cases of benign pleomorphic adenomas and low-grade mucoepidermoid tumors was five years or more, a large number of benign as well as malignant tumors

were diagnosed within a year after their appearance. Early recognition of intraoral minor salivary gland tumors could be attributed to their superficial location in contrast to those occurring in the substance of the major salivary glands.

TABLE II. LOCATION

TUMOR TYPE	PALATE	BUCCAL MUCOSA	LIP			TONGUE*	JAWS	NOT SPECIFIED
			U	L	NOT SPECIFIED			
I. Benign								
Pleomorphic adenoma	27	2	3	0	1	1	2	4
Papillary cystadenoma	0	1	0	0	0	1	1	0
Total	27	3	3	0	1	2	3	4
II. Malignant								
Pleomorphic adenoma	3	0	0	0	0	0	0	0
Adenocarcinoma	7	3	0	1	1	3	1	1
Cylindromatous adenocarcinoma	10	3	1	1	0	1	2	1
Mucoepidermoid tumors	5	3	0	0	0	2	0	0
Undifferentiated carcinoma	1	0	0	0	0	0	0	0
Unclassified carcinoma	0	0	1	0	0	0	0	0
Total	26	9	2	2	1	6	3	2
Grand total	53	12	5	2	2	8	6	6

*Includes floor of the mouth.

Of 1,320 tumors reported in the literature, 800 were benign and 520 were malignant, indicating a higher incidence of the benign series. This finding was further supported by the fact that all mucoepidermoid tumors, irrespective of their histologic features, were counted as malignant. Pleomorphic adenoma was the most common tumor arising from the minor salivary glands, constituting nearly 56 per cent of all tumors of such origin. Cylindromatous adenocarcinoma was the most frequent malignant tumor, but it ranked next to pleomorphic adenoma, comprising an incidence of 16 per cent. Mucoepidermoid tumor was first described as a separate entity in 1945. It constituted an incidence of 10 per cent of 1,106 cases of intraoral minor salivary gland tumors reported since that time. The exact incidence of adenocarcinoma could not be determined with certainty, since Watson[154] considered all tumors of minor salivary gland origin

TABLE III. BENIGN TUMORS AND THEIR LOCATION (1927-1960)

TUMOR TYPE	PALATE	LIP			CHEEK	TONGUE	JAWS	OTHERS	NS	TOTAL
		U	L	NS						
Pleomorphic adenoma	476	105	13	15	38	18	40	22	6	733
Adenoma	15	2	0	0	0	4	0	0	0	21
Myoepithelial adenoma	12	1	0	0	4	0	0	0	0	17
Papillary cystadenoma	9	1	0	0	4	1	0	1	0	16
Canilicular adenoma	1	0	0	2	1	0	0	0	0	4
Fibro-adenoma	3	0	0	0	0	0	0	0	0	3
Cystadenoma	1	0	0	0	0	0	1	0	0	2
Onkocytoma	0	0	0	0	0	1	1	0	0	2
Mucocyst adenoma	2	0	0	0	0	0	0	0	0	2
Total	520	108	13	17	47	24	42	23	6	800

malignant and designated them as adenocarcinomas. Similarly, Martin[97] did not subclassify adenocarcinomas in his series into different types. The palate was the site of predilection for both benign and malignant tumors. The second most common location for pleomorphic adenoma was the lips, the incidence being ten times higher in the upper than in the lower lip. Similarly, the second most common locations for cylindromatous adenocarcinoma and mucoepidermoid tumor were the tongue and third molar regions of the jaws, respectively (Tables III and IV).

TABLE IV. MALIGNANT TUMORS AND THEIR LOCATION (1927-1960)

TUMOR TYPE	PALATE	LIP			CHEEK	TONGUE	JAWS	OTHERS	NS	TOTAL
		U	L	NS						
Cylindromatous adenocarcinoma	104	6	1	5	17	62	12	2	6	215
Mucoepidermoid tumors	43	0	0	2	15	23	22	0	2	107
Adenocarcinoma	69	2	0	12	15	19	4	0	8	129*
Pleomorphic adenoma	13	1	0	0	5	0	5	0	2	26
Papillary cystadenocarcinoma	3	0	0	0	0	1	1	0	0	5
Mucus-producing adenocarcinoma	0	1	0	0	0	0	0	0	2	3
Serous-cell adenocarcinoma	1	0	0	0	0	0	2	0	0	3
Acinic-cell adenocarcinoma	1	0	0	0	0	0	0	0	0	1
Squamous-cell carcinoma	1	0	0	0	2	0	0	0	0	3
Unclassified	7	1	0	0	2	6	0	0	2	18
Undifferentiated	1	0	0	0	0	0	1	0	1	3
Unstated	0	0	0	0	0	0	0	0	7	7
Total	243	11	1	19	56	111	47	2	30	520

*Includes thirty-nine cases reported by Watson, who considered all tumors of minor salivary gland origin as adenocarcinoma, and sixteen cases reported by Martin, who did not subclassify adenocarcinoma.

PLEOMORPHIC ADENOMA

Present Series.—

Clinical findings: In our series pleomorphic adenoma constituted 93 per cent of the benign tumors and 43 per cent of the total of ninety-four intraoral minor salivary gland tumors. The palate was the site of predilection, with nearly 60 per cent of the tumors occurring in this location. The neoplasm affected 21 women and 15 men, suggesting the possibility of a higher incidence in women. The youngest patient was 17 years of age and the oldest 81, the average age being 46.2 years. Although this tumor occurred in all age groups, the incidence was highest in the third decade. In twenty-one patients tumors had been present from seven weeks to ten years prior to diagnosis, the median duration being five years.

The tumor was usually pseudoencapsulated, well-defined, soft to firm in consistency, and covered by normal oral mucosa. Ulceration was exceedingly uncommon and, when present, was usually secondary to trauma. The most common and consistent symptom was a painless swelling which was usually mobile when located in the loose tissues of the lips, buccal parieties, or floor of

the mouth. No such mobility could be found when the tumor occurred in the palate or alveolar ridge, however, because of the tightness of the overlying tissues. Not uncommonly, inability to wear dentures was the initial symptom which brought this lesion to the attention of an edentulous patient. There were some instances in which the patient was unaware of the tumor's presence until the lesion was detected accidentally during a routine intraoral examination. Other symptoms were directly related to the location of the tumor; for example, when there was a tumor in the posterior part of the oral cavity, such symptoms as dysphagia and dysphonia were present.

Roentgenographically, a tumor located next to the palatal bone or the alveolar ridge sometimes caused a regular bony radiolucency by pressure resorption of the underlying bone, without any evidence of invasiveness. When the tumor occurred centrally, within the jawbones, it produced a well-defined radiolucency not unlike a cyst or benign tumor.

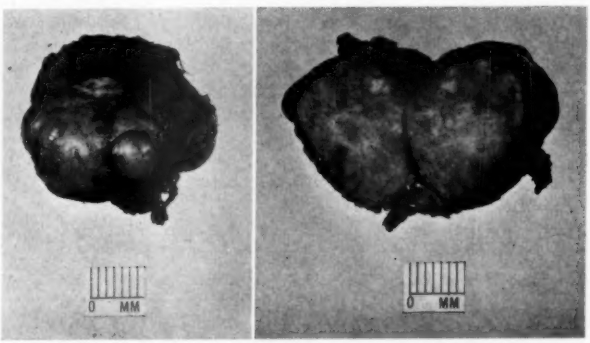

Fig. 1.—Photograph illustrating a well-limited, round, nodular, firm, pleomorphic adenoma removed from the palate. Note grayish, smooth, and shiny cut surface.

Pathology: Grossly, pleomorphic adenomas were usually well defined, but an occasional tumor exhibited a diffuse pattern. These tumors were round or oval and varied in consistency from soft and fluctuant to firm and rubbery, depending upon the presence of cystic or mucoid degeneration or the formation of chondroid or osteoid tissues. When cut, the surfaces were usually smooth, shiny, and glistening, and light gray in color (Fig. 1). It was not unusual for one or more cystic spaces filled with mucoid material to be present.

Microscopically, not unlike pleomorphic adenoma of the major salivary glands, these tumors presented extremely diverse compositional and structural patterns. This diversity was remarkable not only in different tumors but also in different parts of the same tumor. This discouraged further subclassification of pleomorphic adenomas into such varieties as fibroadenoma, canalicular adenoma, myoepithelial adenoma, and so forth. The two essential components of pleomorphic adenomas were epithelial and stromal elements.

The epithelial components showed variation in size, shape, and arrangement of cells. The cells were usually round, oval, or polyhedral, but occasionally they

assumed a spindle shape. Usually there was a relatively large, deep-staining nucleus, contained within an eosinophilic cytoplasm. The cells were scattered singly, sometimes in small nests, occasionally in anastomosing cords, or in groups (Fig. 2). Sometimes they formed ducts and acini lined with cuboidal, columnar, stratified, or pseudostratified epithelial cells. The lumina of the ducts occasionally contained mucicarmine-positive material or cellular debris.

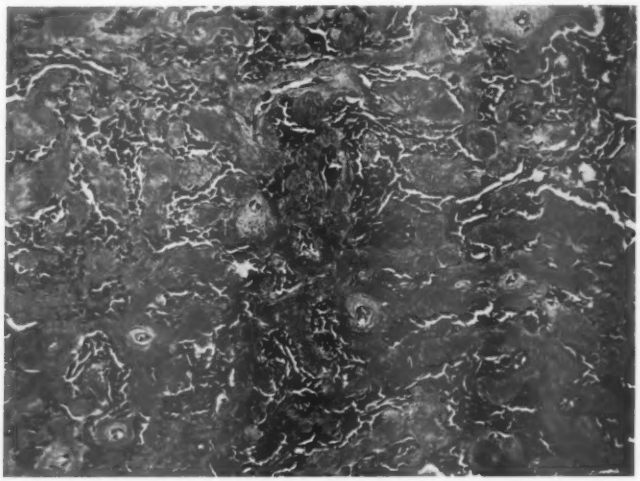

Fig. 2.—Photomicrograph showing typical benign pleomorphic adenoma. Note dense connective tissue stroma interspersed with strands of epithelial cells.

The most common stromal element was dense, hyalinized, eosinophilic connective tissue. Next in order of frequency were myxoid, chondroid, and osteoid tissues (Fig. 3). Transformation of epithelial cells into myxoid and chondroid tissue was quite evident. It appeared that the epithelial tumor cells, through their secretion and subsequent incorporation into it, imparted a chondroid appearance to the tumors. The stromal elements varied in amount from a few strands, as was seen in adenomas, to a large quantity with only a few epithelial cells.

Occasionally the tumors contained areas of squamous metaplasia with keratohyalin formation (Fig. 4) or myoepithelial or cylindromatous elements. In one case the tumor was initially diagnosed as oxyphilic granular-cell adenoma (oncocytoma), but further sectioning of the tissue block revealed typical pleomorphic adenoma.

Treatment and prognosis: In our series, treatment consisted of (1) excision of the tumor mass and the overlying mucosa, or (2) enucleation. In no case was radiation therapy administered. As could be ascertained from the operative notes, no radical treatment was received by any patient. No untoward complications were recorded, except for one case in which perforation of the palate followed excision of the tumor.

The tumors responded favorably to adequate excision or enucleation. In thirty cases the current status could be ascertained. Twelve patients were followed for five years or more without local or distant evidence of the disease.

Fig. 3.

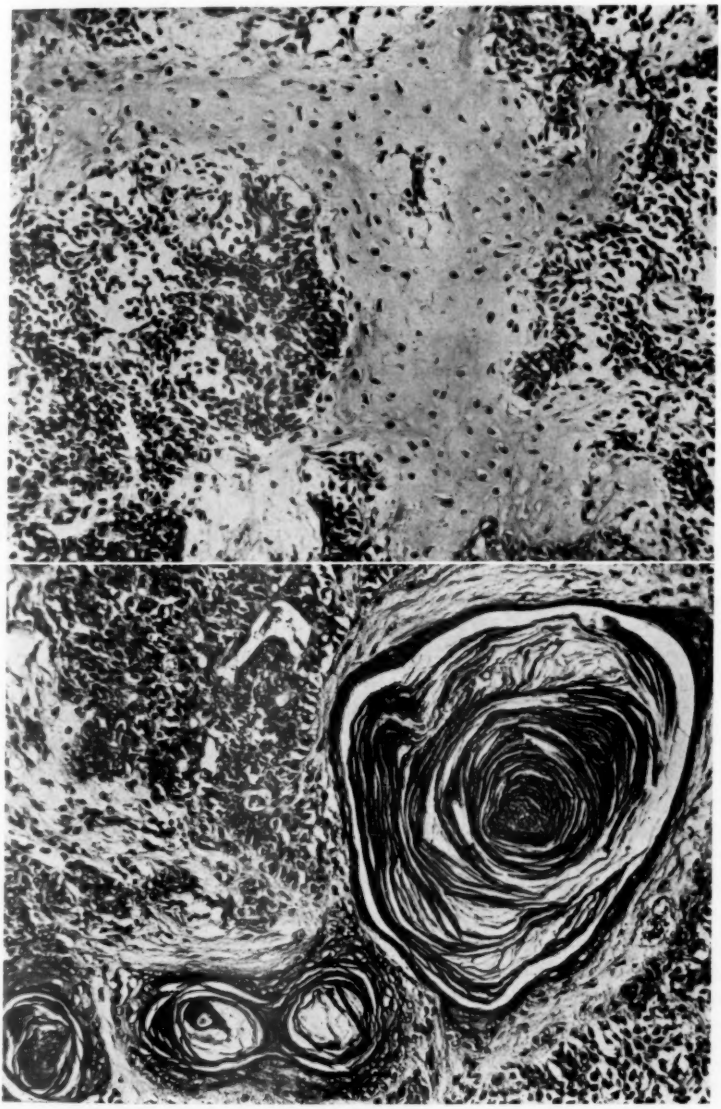

Fig. 4.

Fig. 3.—Pleomorphic adenoma. Note transition of epithelial cells into chondroid stroma.
Fig. 4.—Pleomorphic adenoma. Note ducts filled with keratohyaline material.

Sixteen patients followed from one to five years had no recurrence or metastases. Another patient was treated for recurrent pleomorphic adenoma and had no recurrence over a period of seven years. Only one patient developed recurrence two years following excision of the tumor. From the evidence, it appeared that local excision, or even enucleation, was an adequate method of treatment.

Cases Reported Previously.— There were 733 cases of pleomorphic adenoma reported in the literature. The palate was the most common site of involvement, with nearly 60 per cent of the tumors arising in this location. In the 301 cases in which sex was specified, 155 patients were men and 146 were women, suggesting no predilection. Age was recorded in only 176 cases. The youngest patient was 5 years of age and the oldest was 81; the average age was 40.5 years. Three-fourths of the patients, irrespective of sex, were from 21 to 60 years of age. The duration of the lesion prior to its diagnosis was specified in 114 cases; the range was from 1 week to 39 years, with an average of 67.5 months. Surprisingly, in 42 per cent of the cases the tumor had been present for one year or less. This finding confirms our previous impression from ninety-four cases that intraoral minor salivary gland tumors are detected earlier than major salivary gland tumors. Seventeen per cent of the tumors had been present for more than ten years. The smallest lesion reported was 0.7 cm. and the largest 12.5 cm., the average size being 2.2 cm.

Treatment and prognosis: Unfortunately, individually documented cases lacked adequate follow-up. Only twenty cases were followed for more than five years, and an additional thirty-nine were followed for less than five years. There were eleven cases[6, 14, 47, 52, 57, 60, 61, 68, 103] in which the tumors had recurred one or more times. It would be erroneous to concude from these figures that benign pleomorphic adenoma showed a marked tendency to recur. Perhaps it was more tempting to publish reports of tumors which recurred. A better insight into the behavior of benign pleomorphic adenoma might be gained from the larger series of cases reported by some investigators. Ranger[115] reported the highest incidence of recurrence in his collection of twenty-one patients with such tumors. Of eight intrapalatal tumors treated by enucleation, four recurred two, seven, fourteen, and seventeen years after initial treatment, and the remaining four patients were free of the disease for one, two, twenty, and twenty-seven years, respectively. One patient with involvement of the lip treated by enucleation developed four recurrences over a sixteen-year period. An additional five patients were treated by wide excision, and an equal number were treated by diathermy. However, they were not followed for a reasonable length of time. One intrapalatal tumor was treated by radiotherapy but recurred immediately. Vellios and Shafer[151] reported a recurrence rate of 19 per cent in their series of twenty-one patients. On the other hand, Harrison[78] reported no recurrence in his series of twenty-seven cases. Twenty-one of his patients were alive without recurrence four to sixteen years after being treated by enucleation (extracapsular dissection), three patients died of unrelated causes, and three others could not be traced. Similarly, in the series of thirteen cases reported by Brown and associates,[25] ten patients were treated for more

than five years and were free of recurrence. Treatment consisted of local excision with removal of a margin of normal tissue. Fine and his colleagues[63] reported no recurrence in their twenty-five patients, thirteen of whom were followed for five to thirty years. These patients were treated either by enucleation or by local excision which included the overlying mucosa. Their findings were substantiated by our results.

In conclusion, enucleation (extracapsular dissection) appeared to be a satisfactory treatment. In cases in which there is clinical or microscopic evidence of capsular invasion, however, local excision with removal of a margin of normal surrounding tissue and overlying mucosa appears to be an adequate method of treatment. Radical excision or radiotherapy is not indicated in the management of pleomorphic adenoma.

PAPILLARY CYSTADENOMA

Present Series.—Only three of the ninety-four tumors in our series could be classified as papillary cystadenoma. In the first case the tumor was removed from the buccal sulcus in a 64-year-old white man and was present within hyperplastic tissue which resulted from chronic irritation of an ill-fitting denture. The tumor was composed chiefly of dilated cystic spaces lined with pseudostratified columnar epithelial cells with a pinkish cytoplasm and oval, dark-staining nuclei. Interspersed between the columnar cells were gobletlike cells. The cystic spaces were filled with papillary projections which were also made up of tall columnar cells and supported by thin connective tissue stroma. In close association with the tumor were minor salivary glands, suggesting that the lesions originated from such structures.

The tumor in the second case was removed from the floor of the mouth, where it was incorporated in redundant tissue which had appeared following excision of an ulcer several years previously. This tumor was made up of a large cystlike cavity lined with tall, eosinophilic granular epithelial cells, not unlike oncocytes, which were thrown into papillary projections filling the lumen (Fig. 5). The ductal origin of the lesion was quite apparent.

The third tumor occurred in the mandible in connection with an unerupted premolar, presumably arising from misplaced minor salivary glands.

Cases Reported Previously.—No valid conclusion could be drawn from the nineteen available cases in the literature.[2, 13, 20, 24, 25, 34, 83, 134, 145, 151] Two tumors recurred, and six were reported to have had no recurrence. Whether to attribute the recurrence in two cases to the aggressive nature of the neoplasm, as has been suggested by some,[24] or to inadequate removal is debatable. Nearly one-half of the tumors occurred in the palate; the other sites of involvement were the buccal mucosa, the tongue and its immediate environs, the upper lips, and the mandible. The patients ranged in age from 15 to 78 years; the average age was 47.5 years.

Bauer and Bauer,[13] in discussing the origin of this tumor, suggested the ductal epithelium, principally the relatively undifferentiated epithelium of intercalated ducts, as the possible sites from which the tumor might arise.

MYOEPITHELIAL ADENOMA

No authentic case of myoepithelial adenoma was found in our series. However, seventeen cases were reported in the literature. These were contributed by Bauer and Fox,[12] Bhaskar and Weinmann,[20] Vellios and Shafer,[151] and Fine and colleagues.[63] Twelve tumors originated in the palate, four in the cheeks, and one in the upper lip. Myoepithelial adenoma of minor salivary gland origin was first described by Bauer and Fox,[12] who designated it as "adenomyoepithelioma." They considered it, generally, a benign tumor which could become cancerous, in which case Bauer and Bauer,[13] in their subsequent publication, preferred to call it "myoepithelial adenocarcinoma." Microscopically, the tumor consisted of slender fusiform cells with spindle-shaped or ovoid nuclei. These cells formed interlacing strands of cords arranged in adenomatous fashion. The stroma usually consisted of hyalinized connective tissue in varying amounts. From all available evidence, it appears that myoepithelial adenoma is a variant of pleomorphic adenoma with similar clinical behavior and prognosis.

MALIGNANT PLEOMORPHIC ADENOMA

Only three tumors in our series could be classified as malignant pleomorphic adenoma. Except for an epithelial component which exhibited a sufficient degree of atypism, mitotic activity, and invasiveness, they had all the attributes of pleomorphic adenoma to justify their classification as malignant tumors.

The tumors affected two men and one woman, aged 23, 78, and 92 years, respectively. All three tumors were located in the palate, and they varied in size from 1.0 cm. to 5.0 cm. The chief symptom was a painless swelling. Ulceration was noticed in only one patient. The duration of symptoms ranged from nine months to six years, with no history of a recent rapid increase in size.

Microscopically, the tumors were extremely cellular; the cells were arranged in sheets, with no definite pattern or architecture (Fig. 6). The cells exhibited moderate pleomorphism, and the nuclei varied in size and stained deeply. In one case mitotic activity was quite prominent; in the other cases, although present, mitotic activity was not nearly so marked. In one case there was definite evidence of capsular invasion by the tumor cells. In all instances the stroma was scant and consisted of deeply eosinophilic, hyalinized, collagenous connective tissue.

All three tumors were excised surgically. One patient developed a recurrence at the end of one year. The other patient seemed to be free of the disease but was followed for only one year. The third patient died of an unrelated disease after three years and had no evidence of recurrence at that time.

Cases Reported Previously.—Only twenty-six cases of malignant pleomorphic adenoma of the minor salivary glands were reported in the literature by thirteen authors[9, 25, 29, 52, 57, 62, 64, 67, 87, 100, 106, 143, 147, 152] from 1927 to 1960. The number of published cases would indicate that malignant pleomorphic adenoma was rare. In more than one-half of the cases the tumor occurred in the palate. Of the twenty-six patients, twelve were men, and eight were women, and the sex of the other six was not specified. In eighteen patients there was an age range of 20 to 92 years; the average age was 48 years.

Fig. 5.

Fig. 6.

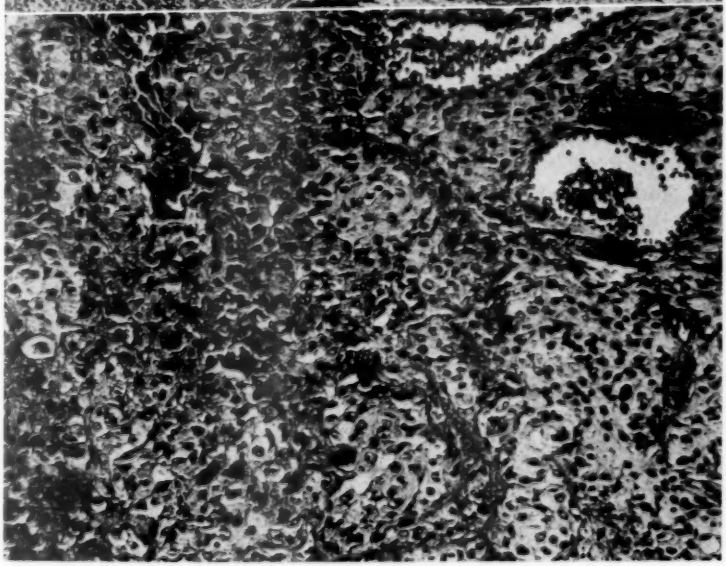

Fig. 5.—Papillary cystadenoma (low magnification). Note dilated ducts filled with papillary projections lined by tall columnar cells.
Fig. 6.—Malignant pleomorphic adenoma. Note extreme cellularity, hyperchromatism, and moderate pleomorphism.

Objective evaluation of the clinical behavior of this tumor was impossible, since the number of well-documented cases was insufficient. Furthermore, it appeared that in most instances a tumor was designated as a malignant pleomorphic adenoma only when it recurred and/or metastasized. It is conceivable that this could have biased the data in terms of prognosis. Recurrences were reported in five cases.[29, 52, 57, 62, 143] Burford[29] and Stoll[143] each reported metastases in two cases.

CYLINDROMATOUS ADENOCARCINOMA

Present Series.—

Clinical findings: In our series of ninety-four cases cylindromatous adenocarcinoma constituted 37 per cent of the malignant tumors but only 20 per cent of all tumors of intraoral minor salivary gland origin. It was quite evident from the data that this was the most common type of malignant tumor, but that it ranked second to benign pleomorphic adenoma. The tumor affected ten men and eight women between the ages of 29 and 81 years. The highest incidence of the disease occurred in the seventh decade, the average age of the patients being 57.5 years. This was more than ten years higher than the average age of patients with pleomorphic adenoma. Location of the tumors was listed in only eighteen cases; more than half of them occurred in the palate. Duration of the tumors prior to diagnosis was mentioned in only twelve cases and ranged from ten days to thirty-five years, but in 90 per cent of the cases it was one year or less.

When located in the palate, the tumors were usually described as firm and infiltrating and occurring on one side of the midline. Invasion of the overlying mucosa by the tumor cells occasionally resulted in ulceration but was by no means a consistent observation. Similarly, pain was more frequently encountered in such tumors but, again, was not as common as that described in cylindromatous adenocarcinoma of the major salivary glands. Involvement of the underlying bone, causing perforation of the palate and extension of the disease into the adjoining structures, was not an unusual feature. When located in places other than the palate, the tumors were usually diffuse, infiltrating, and immobile. Other symptoms caused by the tumors were numbness due to invasion of the regional nerve, dysphagia, and bleeding.

Pathology.—Grossly, when circumscribed, cylindromatous adenocarcinomas were indistinguishable from pleomorphic adenoma. They were relatively firm and were grayish white to yellowish white in color. The cut surfaces were generally homogenous, with relatively little tendency toward cystic degeneration or hemorrhage.

Microscopically, the classic histologic features were their monocellularity and characteristic honeycomb arrangement of the cells (Fig. 7). The cells were uniform in size and shape and contained a relatively large, round hyperchromatic nucleus surrounded by scant cytoplasm. The cells, one to several layers thick, surrounded cystlike spaces of varying sizes. The spaces were either empty or contained mucus, hyaline, or mucohyaline material. Occa-

sionally, the cells formed typical glandular structures resembling ducts and acini. In some instances, the tumors were composed of solid masses of uniform epithelial cells separated by intervening connective tissue stroma. In other instances, they were scattered singly or in small, slender, anastomosing cords

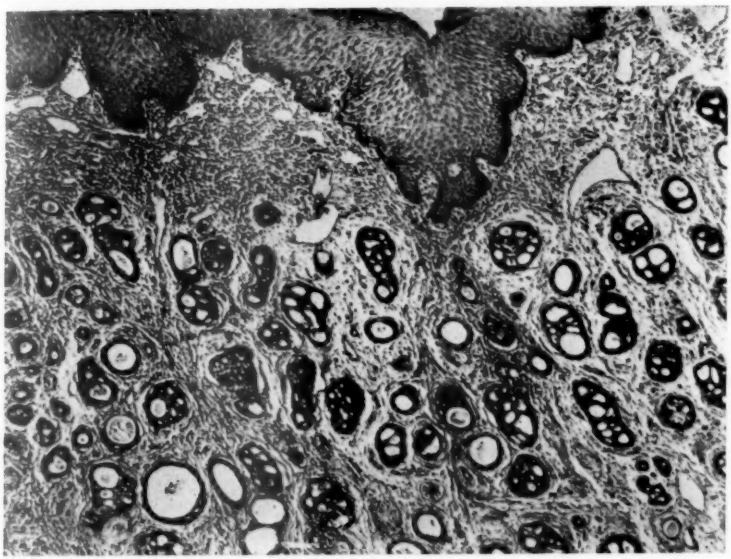

Fig. 7.—Cylindromatous adenocarcinoma. Note typical honeycombed arrangement of cells.

throughout the stroma (Fig. 8). Another very interesting pattern of cylindromatous adenocarcinoma of the oral cavity superficially resembled ameloblastoma (Fig. 9). The epithelial cells were arranaged in broad sheets enclosing cystlike spaces. However, absence of stellate reticulum in such tumors helped to differentiate them from ameloblastoma. Invasion of the surrounding connective tissue by neoplastic cells was a very common finding, but perineural extension of the tumors could not be identified from the available sections. In this series, mitotic activity was negligible except in tumor of the pseudoameloblastic type, in which it was easily demonstrated. The stromal elements of the tumor were variable in quantity as well as in quality. Usually the stroma assumed a myxoid appearance. No chondroid or osteoid stromal elements were present in any of the neoplasms of this type.

There was evidence that cylindromatous adenocarcinoma originated from the ducts and acini of the intraoral mucous glands. A transition from normal glandular components to neoplasia was easily demonstrated. Neoplastic proliferation of the cells lining both ducts and acini resulted, in some instances, in their complete obliteration as they formed solid masses of cells. In other instances, they enclosed spaces and gave a Swiss-cheese pattern to the tumor or they mimicked glands and ducts. In the pseudoameloblastic variety, multiplica-

tion of neoplastic cells resulted in broad sheets with central areas of degeneration resembling ameloblastoma. Hyalinized or myxoid stroma appeared to be a response of the surrounding connective tissue to the tumor cells and their secretory products.

Treatment and prognosis: Three patients had succumbed to regional or distant metastases of the disease. One patient died of an unknown cause. Five patients were living but had the disease in the form of either local recurrence,

Fig. 8.

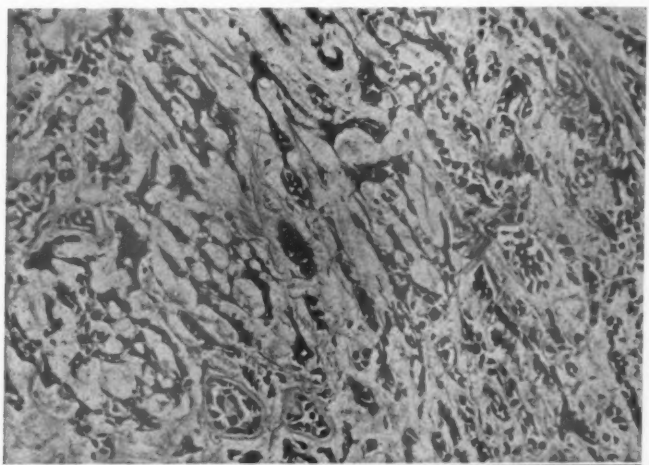

Fig. 9.

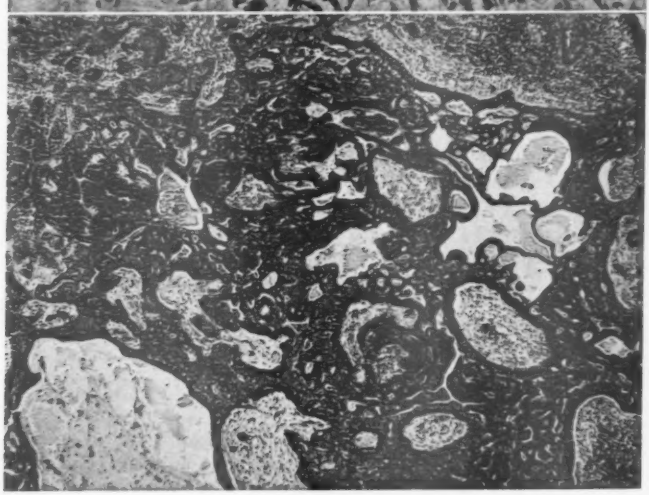

Fig. 8.—A variant of cylindromatous adenocarcinoma in which cells are distributed in slender cords throughout myxoid connective tissue stroma.

Fig. 9.—Cylindromatous adenocarcinoma mimicking ameloblastoma. Note, however, the absence of stellate reticulum.

regional or distant metastases, or both. Two of these five patients lived for more than five years; they were initially treated by wide surgical excision, but the tumors were kept under control by radiation therapy. Five patients had no evidence of the disease; three of these were followed for less than three years and two for more than five years. The last two patients were treated by wide surgical excision. No information could be obtained concerning six patients.

Cases Reported Previously.—The 215 cases reported by twenty-nine contributors[3, 13, 15, 25-28, 43, 57, 63, 67, 70, 79, 80, 88, 98, 103, 104, 115, 116, 119, 123, 124, 131, 135, 137, 149, 151, 155] from 1927 to 1960, constituting 16 per cent of all intraoral minor salivary gland tumors. This finding is in close agreement with the findings of Vellios and Shafer[151] and Fine and associates,[63] who reported an incidence of 15 per cent and 16.5 per cent, respectively. Others reported a higher incidence, ranging from 25 to 50 per cent.[79, 103, 115] It appeared that the relative incidence of cylindromatous adenocarcinoma was higher in the intraoral minor salivary glands than in the major salivary glands. Nearly 50 per cent of the tumors occurred in the palate, the tongue being the second most common site of involvement. The sex of the patients was specified in 115 cases; sixty-four patients were women and fifty-one were men, indicating a slightly higher incidence in women. Age was recorded in only fifty-nine cases. The youngest patient was 16 years of age and the oldest was 85, the average being 52 years. The mean age of women was six years higher than that of men. Nearly 75 per cent of the patients were in 41- to 70-year age group. Duration of the tumor prior to diagnosis was listed for thirty-five patients; this ranged from a few weeks to twenty-one years, with an average of thirty-six months. In 45 per cent of the patients, the tumor was recognized within one year. Pain and ulceration were stressed by Burbank and co-workers[28] as diagnostic features of cylindromatous adenocarcinoma of the tongue.

Treatment and prognosis: Since there was a wide variation in which different investigators presented end results in their patients, it was deemed necessary to quote them separately.

In Ranger's[115] series, three patients with intrapalatal tumors developed several recurrences. One of them died after five years, another had extensive local recurrence with pulmonary metastases after seven years, and still another had several recurrences during the last eleven years. Of seven patients with lingual tumors, three died of local recurrences and one died of unknown causes. The remaining three patients were apparently well and living from three to four years after treatment; one of them was treated by wide local excision and two with teleradium. Harrison[79] reported that death followed recurrence of tumors in twenty-four of his thirty-six patients, and all except one of these deaths occurred within seven years following treatment. Three other patients died of unrelated causes. Four patients were alive but had inoperable recurrences of their tumors. There were only three patients who were living and well for four, nine, and ten years, respectively. Six patients developed cervical metastases and six distant metastases, chiefly to the lungs, bones, and liver. The distant metastases had occurred up to five years after treatment. Burbank

and associates,[28] discussing twenty-two cases of cylindromatous adenocarcinoma of the tongue, reported that thirteen patients died two days to nine years after treatment, the other nine patients were apparently well and living fourteen months to thirteen years after surgical excision of the tumors. Three patients developed metastases to the liver and lymph nodes in the course of the disease. In thirteen cases described by Fine and colleagues,[63] local recurrence and metastases at intervals of four months to four years, developed in nine patients. Two patients were living, with no evidence of tumor, less than one year after excision. No patient lived free of the tumor for five years. Ten patients were treated by surgical excision (which included the overlying mucosa), one received radiation treatment, and one refused treatment. Only four patients required removal of adjacent bone. In addition, recurrences were reported in twenty-one other individually documented cases.[3, 15, 26, 27, 88, 103, 119, 123, 135, 151, 155] Metastases were recorded in five additional patients.[26, 27, 57, 88, 155]

In conclusion, the literature indicated that cylindromatous adenocarcinoma was a locally infiltrating tumor with a marked tendency to recur. Metastases to regional lymph nodes and distant organs—chiefly lungs, bones, and liver—were not uncommon. Treatment consisted primarily of wide surgical excision, but radiotherapy alone or in combination with surgical intervention also seemed effective. There was strong evidence that radiotherapy was helpful, especially in temporarily arresting the growth of primary as well as secondary tumors.

MUCOEPIDERMOID TUMORS

Present Series.—

Clinical findings: There were ten mucoepidermoid tumors (seven of low-grade and three of high-grade malignancy), constituting 11 per cent of the ninety-four intraoral minor salivary gland tumors in our series. This is in complete agreement with the findings of Murphy,[103] who reported nine cases of such tumors in his series of seventy-nine patients. A higher incidence has been reported by other investigators.[20, 63, 135] It appeared from the reported series that the relative incidence of mucoepidermoid tumors in intraoral minor salivary glands is higher than that reported in the major salivary glands (5 per cent).

The palate was the most common site of involvement. Five of the tumors occurred in this location; four of these were peripheral and one was central in origin in the third molar region. The youngest patient was 16 years of age and the oldest 70 years; the average age was 51.9 years. The average age in seven patients with low-grade tumors was only 45 years, compared to an average age of 64 years in three patients with tumors of the high-grade variety. The median duration was seventy-two months in the former, as compared to twelve months in the latter. The tumors affected men and women equally.

Clinically, the tumors (chiefly the low-grade type) were indistinguishable from benign pleomorphic adenoma. The most characteristic symptom was a painless swelling, with a consistency depending upon the location and the amount of mucus secretion by the tumor. In one instance there was a fistulous tract from which mucus could be expressed. The low-grade tumors were

usually well-limited, with or without the presence of a capsule. The high-grade tumors were diffuse and gave no evidence of ulceration of the overlying mucosa. There was no instance of bony involvement.

Pathology: Grossly, low-grade mucoepidermoid tumors were similar to pleomorphic adenoma except for the presence of cavitation due to necrosis in an occasional case. The high-grade tumors were diffuse and infiltrating. Microscopically, the low-grade mucoepidermoid tumors were well differentiated and consisted of large ducts, the lumina of which were dilated not uncommonly to the extent of formation of cysts filled with amorphous material. The principal cellular components lining the ductal walls were epidermoid cells, mucus-producing cells, and intermediate or basal cells. The intermediate cells were distinctly smaller than either epidermoid or mucus-producing cells. The epidermoid cells were large and polygonal, with vesicular nuclei and abundant, eosinophilic cytoplasm. In addition to mucus-producing cells, some of the tumors contained large hydropic or clear cells which were not productive of mucus (Fig. 10). In low-grade tumors, the intermediate cells were less conspicuous. The epidermoid and mucus-producing cells were almost equally common. In some instances, the tumors consisted of solid masses of epidermoid, mucus-producing, and intermediate cells without lumina. Areas showing transition from intermediate to epidermoid and mucus-producing cells could be identified. A spillage of mucus into the surrounding tissues was accompanied by an inflammatory reaction.

The high-grade tumors were characterized by the predominance of epidermoid and intermediate cells and relatively few mucus-producing or clear cells (Fig. 11). Two tumors appeared to be growing as solid masses within large ducts. Mitotic activity was present but was not prominent. In one case the tumor had the morphologic features of a papillary cystadenocarcinoma, but the ductal lining and papillary projections were composed of large numbers of mucus-producing epidermoid, and intermediate cells.

Schilling[125] was the first to suggest that mucoepidermoid tumors might arise from the largest terminal ducts of the salivary glands. Skorpil[133] attributed their origin to the basal cells lining the isthmus of the excretory duct. These cells, according to him, have the potentiality to differentiate into epidermoid and mucus-producing cells. Stewart and associates[140] suggested that the tumors might arise from those portions of the duct system that are proximal to the lobules, since at this point the lining cells of the salivary ducts become eosinophilic and cells of this character are not present in mucoepidermoid tumors.

Bossart,[22] from his study of two cases of mucoepidermoid tumors of the jawbones, concluded that these tumors might arise from oral epithelium. Barla-Szabo[11] subscribed to his views and demonstrated, histologically, a direct continuity between the surface epithelium and the neoplastic tissue in several tumors of his series. In our opinion, however, this appeared to be the growth of the tumor toward the surface epithelium. Furthermore, in some of our cases the close association of mucoepidermoid tumors with minor salivary glands was convincing evidence of their origin from such structures.

Fig. 10.

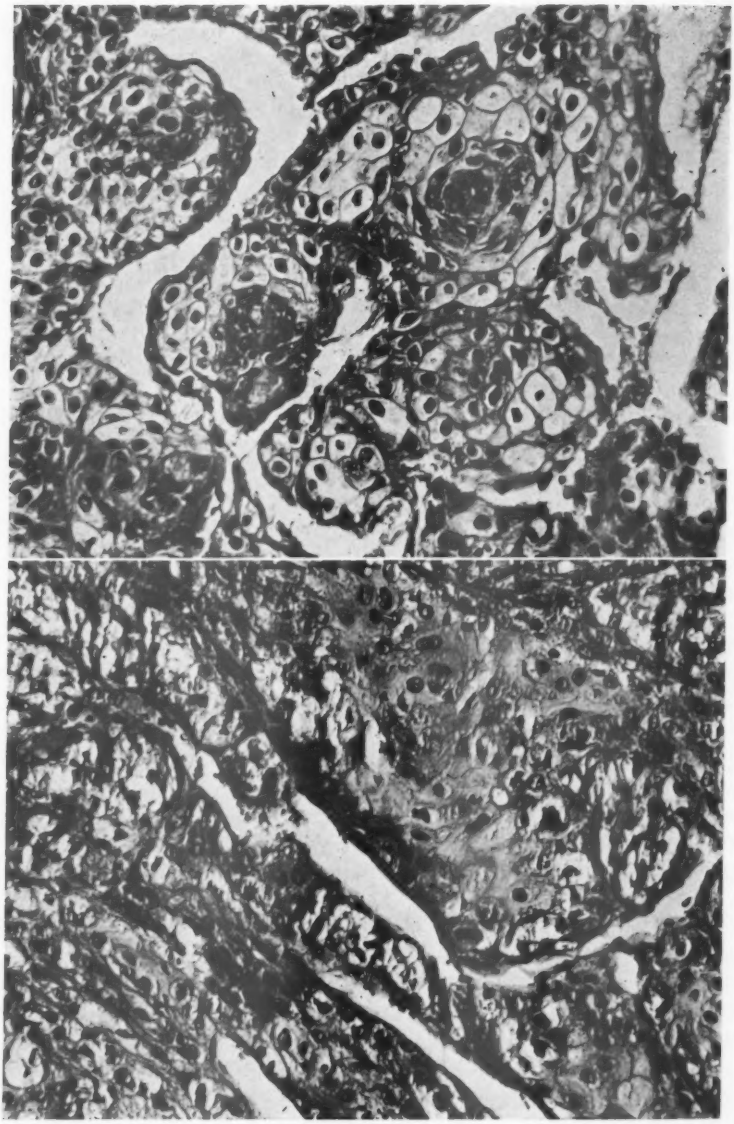

Fig. 11.

Fig. 10.—Mucoepidermoid tumor (low-grade), a hypernephroid type. Note vacuolated cells with relatively small, round nuclei. These cells were negative for mucocarmine stain.

Fig. 11.—Mucoepidermoid tumor (high-grade). Note the predominance of epidermoid and intermediate cells with occasional mucus-producing cells.

Treatment and prognosis: No recurrence was reported in low-grade mucoepidermoid tumors followed for two to twenty years. These tumors were all treated by local excision.

One patient with high-grade mucoepidermoid tumor died of some unknown causes, another patient developed lymph-node metastases but was living, and a third was apparently without any recurrence when last seen one year following surgical excision of the tumor.

Cases Reported Previously.—One hundred seven cases of mucoepidermoid tumor were reported by seventeen investigators[8, 11, 13, 20, 25, 28, 57, 63, 91, 99, 103, 115, 135, 139, 140, 148, 157] from 1945 to 1960. These represent 10 per cent of all intraoral minor salivary gland tumors, compared with the 5 per cent incidence in major salivary glands reported by Foote and Frazell.[66] The palate again was the site of predilection, with about 40 per cent of the tumors arising in this location. Interestingly, more than 20 per cent of the lesions occurred in the jaws, chiefly in the retromolar and tuberosity regions. The sex of the patients was specified in eighty-nine cases. Fifty-four patients were women and thirty-five were men; thus, there was a slightly higher incidence in women. Age was stated in thirty-eight cases. The youngest patient was 16 years old and the oldest was 79, with an average of 46 years; one-half of the patients were between 31 and 50 years of age. Duration of the tumors prior to diagnosis was listed in only twenty-four cases and ranged from two weeks to twenty-eight years, the average being five years. The smallest tumor reported was 0.3 cm., and the largest was 6.0 cm.

Prognosis and treatment: Smith and co-workers[135] reported seven cases of "benign" mucoepidermoid tumors and five cases in which the tumors were malignant. All patients with "benign" tumors, except for one who had one recurrence, were apparently well and living one to five years after treatment. Four of the five patients with malignant tumors had one or more recurrences. Barla-Szabo[11] reported no recurrences in three patients followed for one, four, and five years, respectively, whereas three additional patients had developed one to multiple recurrences. Burbank and associates[28] stated that seven of eleven patients in their series were alive two to twenty-five years after treatment, whereas four others died one to twenty-four years after surgical treatment. Brown and colleagues[25] reported no recurrences in their collection of five mucoepidermoid tumors (four low-grade and one high-grade). Except for one patient who received radiation therapy, all were treated surgically. All were living and apparently well, three of them having been followed for more than five years. Fine and co-workers[63] followed nine of their cases of low-grade mucoepidermoid tumor for one to thirty years and reported one recurrence, presumably due to "incomplete initial removal." Eight tumors were locally excised with overlying mucosa, but in one instance the tumor was removed in fragments. Radiation was combined with excision in two cases. Only one case necessitated partial removal of underlying bone. In the malignant series, six patients were followed for five or more years and four for one year after therapy. Three of the former remained free of tumor for periods ranging from six to eight years. Recurrences and metastases occurred in three and two

patients, respectively. The tumor had apparently spread only to the regional lymph nodes. Eight patients in this group were treated by excision and two by combined excision and radiation therapy. Vellios and Shafer[151] reported recurrence in three of fifteen patients, an incidence of 20 per cent. Five additional cases of mucoepidermoid tumors with recurrence were reported by others.[11, 91, 115] Only one tumor of the tongue metastasized.

In conclusion, it seemed that low-grade mucoepidermoid tumors could be adequately treated by local excision, while those of high-grade malignancy needed wide surgical excision, alone or in combination with radiation therapy.

ADENOCARCINOMA

Present Series.—

Clinical features: There were seventeen cases of adenocarcinoma, comprising 18 per cent of the ninety-four tumors of the intraoral minor salivary glands in our series. In addition to the conventional variety of adenocarcinoma, this group also included such histologic types as papillary (or cystadenocarcinoma), mucus-producing, and trabecular adenocarcinoma. Since there was no convincing evidence that these tumors differed in their clinical behavior, no attempt was made to group each type separately.

Adenocarcinoma affected twelve men and four women, and in one case sex was not specified. The youngest patient was 43 years of age and the oldest was 84; the average age was 61.5 years. Eight tumors occurred in the palate. The median duration in nine patients was only fifteen months.

Pathology: Grossly, the tumors were diffuse and infiltrating. Their consistency varied with the amount of necrosis and hemorrhage present in them.

Microscopically, the tumors showed gradations from well-differentiated to extremely anaplastic types. A well-differentiated, conventional adenocarcinoma usually consisted of well-formed but irregular ducts and acini (Fig. 12). The ductal lining varied from single to multiple layers of moderately hyperchromatic, pleomorphic cells with loss of polarity. The mitotic activity varied with the degree of anaplasia. In the poorly differentiated type, the epithelial cells were usually large, with abundant cytoplasm and large vesicular nuclei containing prominent nucleoli. They were arranged in broad, solid sheets with abortive attempts at formation of glandular structures. Metaplasia of glandular epithelium into the squamous variety and subsequent keratinization were noticed occasionally. Not uncommonly, foci of cylindromatous components could be identified in an otherwise conventional type of adenocarcinoma. The stromal element usually consisted of dense, hyalinized, connective tissue. In papillary varieties of adenocarcinoma, the walls of the dilated ducts were lined with single or multiple layers of tall columnar or cuboidal cells, occasionally interspersed with mucus-producing cells (Fig. 13). The papillary processes were projecting into the dilated lumina. The origin of such tumors from ductal epithelium was quite obvious.

A trabecular adenocarcinoma seen in a 55-year-old white woman had been present for approximately two months. It was nearly 0.5 cm. in size and was located on the right side of the palate in the region of the second and third

molars. The overlying mucosa was ulcerated. A biopsy revealed lobules of densely packed cells which were often arranged in the form of pseudoacini with an occasional true acinus. The lobules were separated by scant connective tissue fibers which occasionally contained dilated vascular channels (Fig. 14). The cells showed very slight variation in size and shape, and they were generally round with centrally placed oval to spindle-shaped vesicular nuclei and

Fig. 12.

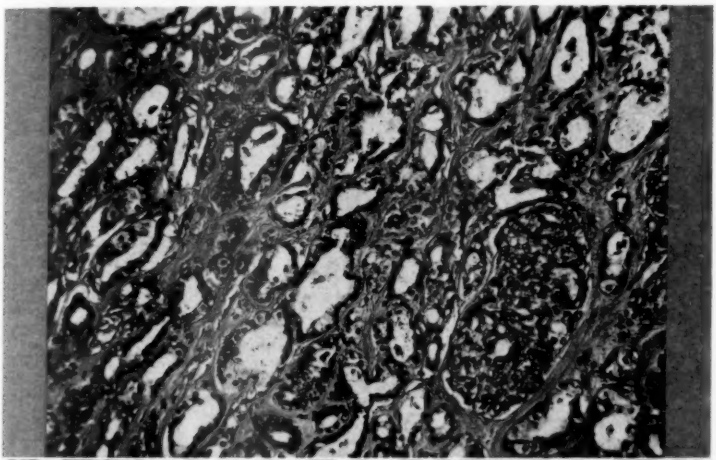

Fig. 13.

Fig. 12.—Adenocarcinoma (conventional type). Note irregular glandular structures lined by hyperchromatic epithelial cells.

Fig. 13.—Papillary cyst adenocarcinoma. The dilated ducts lined by multiple layers of hyperchromatic epithelial cells forming papillary processes projecting into the lumen.

eosinophilic cytoplasm. An occasional mitotic figure was present, with definite evidence of infiltration. The lesion was widely excised with overlying mucosa. The underlying palatal bone was not removed. To date the patient has been followed for only six months, but there has been no evidence of recurrence.

Fig. 14.

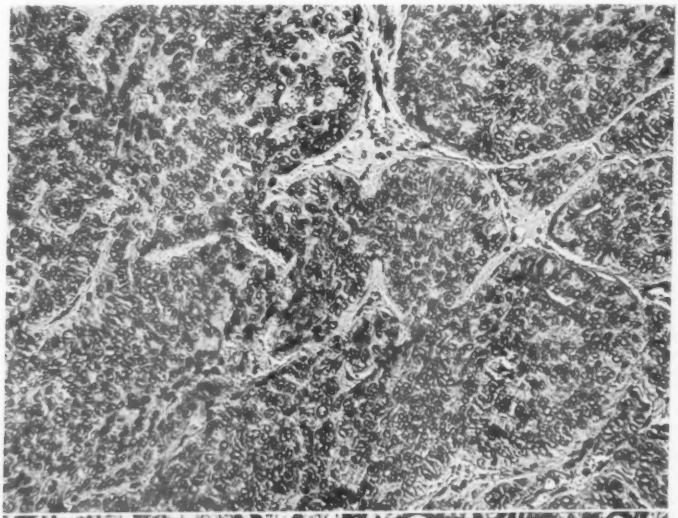

Fig. 15.

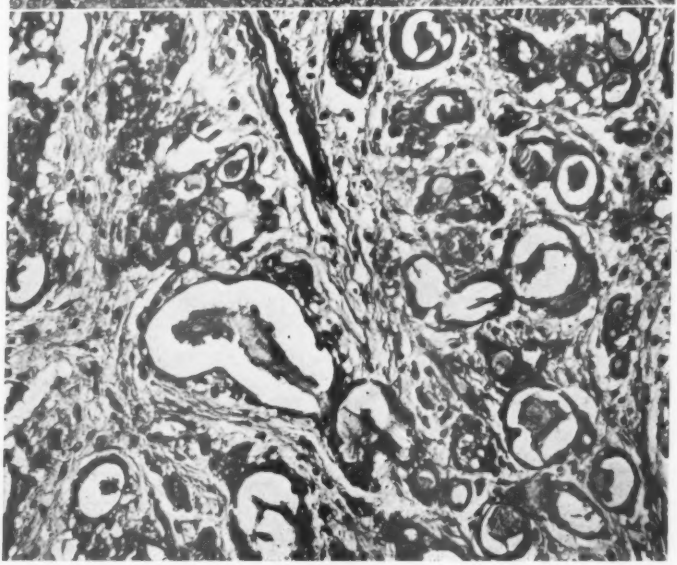

Fig. 14.—Trabecular adenocarcinoma. Note the extreme cellularity and trabecular arrangement of the cells. Mitoses were quite uncommon.

Fig. 15.—Mucus-producing adenocarcinoma. Note the glandular structures lined by hyperchromatic cells. The lumina of these structures were filled with mucus.

A mucus-producing carcinoma occurred in the symphysis of the mandible in a 60-year-old man. It had been present for fifteen to twenty years and had caused gradual expansion of the cortical plate of bone, without perforation. Microscopically, the tumor was composed of a large number of irregular glandular spaces filled with eosinophilic material. The spaces were lined by flat cuboidal cells one to several layers thick (Fig. 15).

Treatment and prognosis: The present status could be ascertained in only ten cases. All but two patients (who have been followed for less than a year) had one or more recurrences. Four patients died of lymph-node or pulmonary metastases. The other four were living and had had several recurrences, with or without lymph-node or distant metastases. The over-all prognosis, irrespective of the mode of treatment appeared grave for this tumor.

Cases Reported Previously.—The adenocarcinomas, except for those of the cylindromatous variety, which were reviewed included seventy-four conventional adenocarcinomas, five papillary, three serous-cell, three mucus-producing, one acinic cell, and three poorly differentiated adenocarcinomas, making a total of eighty-nine cases reported by sixteen investigators.[20, 25, 28, 42, 57, 63, 64, 71, 85, 93, 98, 102, 103, 128, 135, 151] This number, however, did not include thirty-nine cases reported by Watson[154] or sixteen reported by Martin.[97] Unfortunately, the number of well-documented cases was not large enough to yield any reliable information, except for the fact that the palate was the most common site of involvement. Sex was listed in only twenty-two cases; thirteen patients were men and nine were women.

It appeared that adenocarcinoma was the most serious malignant tumor arising from the intraoral minor salivary glands and offered the poorest prognosis, irrespective of the mode of treatment. This was supported by the end results seen in ten cases in our series, as well as those reported by Brown and associates[25] and by Burbank and his colleagues.[28] Brown reported sixteen cases of adenocarcinoma, including four of the cylindromatous variety. Eight of them had developed metastases, including six to such distant organs as the lungs, vertebrae, mediastinum, brain, and skin. Six patients were apparently well and living, but only one of them was followed for more than five years. Among nine cases reported by Burbank and co-workers, five had died within seven months to seven years and the other four were living for three to sixteen years. One patient developed metastases to the cervical chain of lymph nodes. Mumma[102] reported another case in which adenocarcinoma of the base of the tongue metastasized to the nodes.

UNDIFFERENTIATED CARCINOMA

A single case of undifferentiated carcinoma occurred in an 83-year-old white man who complained of a painful, bleeding ulcer on the palate of three months' duration. Biopsy of the lesion revealed the tumor to be composed of extremely undifferentiated cells exhibiting marked mitotic activity. In a few microscopic fields, there was a suggestion that these anaplastic cells were arranged in such a fashion as to mimic glandular structures; however, opinions varied and a final diagnosis was inconclusive.

UNCLASSIFIED CARCINOMA

An additional tumor, diagnosed as an unclassified carcinoma, occurred in a 42-year-old white man who had developed a swelling of the upper lip. The lesion was biopsied and found to be composed of large cells with clear cytoplasm and relatively small, vesicular nuclei. The cell boundaries were distinct and in close contact with one another, with no intervening stroma. The patient developed regional and distant metastases and died of the disease. The tumor appeared to be a metastatic hypernephroma, but this could not be confirmed by the autopsy findings.

DISCUSSION

All tumor types which are found in the major salivary glands also seem to occur in the intraoral minor salivary glands, except for the papillary cystadenoma lymphomatosum. Its absence is easily understandable, in view of its different histogenesis. Foote and Frazell reported 37 per cent malignant and 63 per cent benign tumors in their series of 877 major salivary gland neoplasms. These figures are in close approximation to those found in our survey of intraoral minor salivary gland tumors, which indicated that 39 per cent of the tumors reported from 1927 to 1960 (including ninety-four cases from our collection) were malignant and 61 per cent were benign. A relatively higher incidence of cylindromatous adenocarcinoma and mucoepidermoid tumor in the minor glands could be due to the fact that other malignant tumors, such as squamous-cell carcinoma, are exceedingly uncommon.

Except for a few minor differences, pleomorphic adenomas in both the major and the minor salivary glands exhibit a marked similarity in clinical features, microscopic characteristics, tendency to recurrence, and prognosis. Unlike tumors of the major salivary glands, which are more common in female patients (60 per cent), there is no such apparent sex difference in intraoral minor salivary gland tumors. In addition, there is no indication that the recurrent lesions are most commonly multiple, as in the case of major salivary gland tumors. Histologically, there is a higher incidence of pseudocartilaginous stroma in the tumors of the major glands. There is evidence that the recurrence rate of minor salivary gland tumors is no higher than the 5 per cent reported by Foote and Frazell in primary tumors of the major salivary gland. In fact, the recurrence rate in minor salivary gland tumors may be lower, because of accessibility for treatment, anatomic location, and lack of such complicating structures as the facial nerve. This would encourage much simpler procedures, such as enucleation or local excision in the treatment of pleomorphic adenoma of minor salivary gland origin.

Evaluation of the literature on the subject of malignant pleomorphic adenoma appears impossible. First, there is marked diversity in criteria used by different investigators in their diagnosis of such tumors. This is quite evident from the fact that Murphy[103] and Fine and associates,[63] in their series of seventy-nine tumors each, did not report a single case of malignant pleomorphic adenoma, while Edwards[57] reported three in a series of twenty-three

intraoral minor salivary gland tumors. Second, these tumors are exceedingly uncommon in the intraoral minor salivary glands and therefore not much information is available about them. Third, there appears to have been a tendency to designate as malignant only those tumors which recurred or metastasized.

From the available information, there was no convincing evidence that malignant pleomorphic adenoma arises from previously existing benign pleomorphic adenoma, as is supposedly the case in major salivary gland tumors. It is pertinent to point out that occasionally malignant pleomorphic adenoma is misinterpreted as sarcoma, chiefly chondrosarcoma, and vice versa. The use of the term *malignant pleomorphic adenoma* should be adopted, since it indicates variegated histologic features similar to those of pleomorphic adenoma, except for additional evidence of increased cellularity, mitotic activity, lack of cell differentiation, and invasiveness. Furthermore, the tumor should be viewed as a separate entity because it is conceivable that its clinical behavior and prognosis may be found to be different from adenocarcinoma when more cases become available for study.

Cylindromatous adenocarcinomas of both major or minor salivary glands have several features in common. For example, these tumors occur most frequently in the same age group, and they exhibit a slight predilection for women. They grow relatively slowly but possess a marked tendency to recur and develop metastases to the lymph nodes, lungs, bones, and liver. As a general rule, metastases occur following repeated recurrences and a lapse of a few years after treatment of the primary lesion. However, there are reported cases in which the patients died of metastases in less than a year after the appearance of the primary tumor. No definite correlation could be established between the microscopic features and the clinical behavior of such tumors. Buxton and associates,[31] however, pointed out that the cellular variant of cylindromatous adenocarcinoma is most malignant.

The relative incidence of cylindromatous adenocarcinoma in the intraoral minor salivary glands ranges from 14 per cent to 50 per cent,[63, 78, 151] compared with 5 per cent to 10 per cent in the major salivary glands.[66, 116] From the available literature, it it our impression that cylindromatous adenocarcinoma offers a more serious prognosis when it occurs in the oral cavity. The five-year cure rate is less than 25 per cent, as reported by Foote and Frazell,[66] for similar tumors of the major salivary glands. Unfortunately, no percentage cure rate could be obtained for tumors of minor salivary glands because of the great variability with which different investigators presented the end results of treatment in their patients. The difference in prognosis, however, could be attributed to several factors: (1) The tumors are relatively inaccessible for adequate management when they occur in such parts of the oral cavity as the floor of the mouth, the base of the tongue, etc.; (2) the relatively rich lymphatic and vascular drainage of the tongue and its surrounding parts may predispose to an early dissemination of tumor cells to regional nodes and distant organs; (3) the constant trauma to which a malignant tumor may be subjected in the mouth may possibly cause its rapid spread locally or to distant organs; and (4)

extension of the tumor to adjoining complicated anatomic structures (for example, the spreading of a lesion of the palate to paranasal sinuses or the base of the skull) may make its complete eradication exceedingly difficult, if not impossible.

In 1945, when Stewart, Foote, and Becker[140] identified mucoepidermoid tumors as neoplasms constituting a separate entity, they classified them into benign and malignant types on the basis of microscopic appearance. On subsequent follow-up, however, they found that some of the tumors which were designated as benign had not only recurred but metastasized. It was considered logical, therefore, that all mucoepidermoid tumors were malignant to varying degrees. Some were of low-grade and others of high-grade malignancy. Thereafter, several investigators substituted the term *mucoepidermoid carcinoma* in place of *mucoepidermoid tumor*.[91, 160] It is our feeling that some of these tumors in the oral cavity are definitely benign and that others are frankly malignant, but there are some in which the line of demarcation is not distinct. It is this last variety in which the clinical behavior of the tumor may be found at variance with the microscopic interpretation. Therefore, we are inclined to suggest that the term *mucoepidermoid carcinoma* should be used in the restricted sense, for the word *carcinoma* is unnecessarily alarming to patients and its use in a diagnosis may even lead to mutilating operations for tumors which are not malignant. Analysis of data obtained from the literature strongly indicates that the so-called "low-grade mucoepidermoid tumors" of intraoral minor salivary glands are essentially similar to pleomorphic adenoma in their clinical behavior and their tendency to recur or to develop metastases. They respond favorably to adequate local excision. The high-grade type, as in the major salivary glands, is very aggressive, with a marked tendency to recur and to spread to lymph nodes and distant organs.

Finally, for obvious reasons, we failed to collect any additional information on the characteristics of such tumors as trabecular, mucus-producing, anaplastic, or acinic-cell adenocarcinoma. Adenocarcinoma (excluding the cylindromatous variety), as an over-all group, appeared to be the most seriously malignant neoplasm. It offered the gravest prognosis, as was evident from the few well-documented cases in the literature and from seventeen cases in our collection. Surprisingly, 18 per cent of the tumors in our series were adenocarcinomas.

SUMMARY AND CONCLUSION

We have attempted to analyze data on the clinical features, microscopic characteristics, treatment, and prognosis of ninety-four cases of intraoral minor salivary gland tumors from our own collection and 1,320 cases published in the English-language literature from 1927 to 1960, inclusive, making a total of 1,414 cases. This has provided an adequate number of cases of pleomorphic adenoma, cylindromatous adenocarcinoma, and mucoepidermoid tumor to enable us to gain reliable information. Also, it has enabled us to collect useful information on less common tumors, such as papillary cystadenoma, malignant pleomorphic adenoma, and adenocarcinoma. It would be exceedingly helpful if more

investigators would publish their material on this subject for an even better understanding of these lesions.

1. Pleomorphic adenoma appears to be the most common tumor arising from the intraoral minor salivary glands. Next in order of frequency are cylindromatous adenocarcinoma, mucoepidermoid tumor, and adenocarcinoma.

2. Malignant tumors are equally common in the minor and major salivary glands.

3. Benign tumors occur most frequently in the fourth and fifth decades of life, and malignant tumors are most common in the sixth decade.

4. The palate is the site of predilection for all varieties of benign and malignant intraoral minor salivary gland tumors. The next most common sites of involvement for pleomorphic adenoma, cylindromatous adenocarcinoma, and mucoepidermoid tumor are the upper lip, the tongue, the floor of the mouth, and the retromolar regions, respectively.

5. Pleomorphic adenoma is a slow-growing tumor with no unusual tendency to recur. There is no evidence that long-standing benign tumors may undergo malignant transformation. In general, enucleation seems to be an adequate method of treatment. In case of clinical or microscopic evidence of capsular invasion, local excision of the tumor and the overlying mucosa is satisfactory. The prognosis is excellent. Radical surgical excision or radiation therapy is not indicated.

6. From the limited data available, papillary cystadenoma seems to be no different from pleomorphic adenoma in its clinical behavior. However, more reliable information should be forthcoming as more cases are studied.

7. Malignant pleomorphic adenoma, as suggested by the sparsity of reported cases, is quite uncommon in the oral cavity. Its histologic differentiation from sarcoma, especially chondrosarcoma, should be kept in mind. From the small number of available reports, it appears that the tumor is likely to recur and metastasize and, therefore, requires radical excision. The prognosis is guarded.

8. From its clinical behavior and end results, it would appear that the low-grade mucoepidermoid tumor is more common in the oral cavity than the high-grade variety. The low-grade tumors do not tend to recur or metastasize, and adequate local excision should suffice. Prognosis is good. On the other hand, the high-grade type frequently recurs and metastasizes, and the treatment should involve wide excision of the tumor, the overlying mucosa, and the surrounding normal tissue. The prognosis is guarded.

9. Cylindromatous adenocarcinoma exhibits a marked tendency to recur and metastasize to lymph nodes, lungs, bones, and liver. Metastasis usually occurs after a lapse of several years following treatment of the primary tumor. Occasionally, this tumor may be confused on microscopic examination with ameloblastoma. Radical surgical excision alone or combined with radiation is the logical treatment of choice. The prognosis is grave.

10. Adenocarcinoma (conventional type), appears to be the most serious neoplasm arising from intraoral minor salivary glands. It grows rapidly and

seems to have a marked tendency to spread to regional lymph nodes and distant organs. It offers an extremely grave prognosis, irrespective of the mode of treatment.

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RESEARCH

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EFFECTS OF INFERIOR ALVEOLAR NERVE SEVERANCE ON THE ERUPTION RATE OF THE MANDIBULAR INCISOR IN THE 10-DAY-OLD WISTAR ALBINO RAT

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INTRODUCTION

THE literature on the innervation of dental structures, both animal and human, contains a rich record of painstaking work on the anatomic and morphologic aspects of the subject. Fewer studies have been concerned with the functional aspects. We refer here to records on the rate of eruption in animal teeth and to the changes in this rate consequent to nerve severance. Such a study would entail investigations of function (both normal and deranged) and of the mechanisms which operate in its control.

That a neural mechanism is involved in controlling eruption of the incisor tooth of the albino rat has received the attention it deserves from a number of investigators. Taylor and Butcher[1] investigated the effects which variation in diet, alteration in shape, application of stress, alteration in blood supply, and finally denervation have on the eruption rate of the incisor in the white rat. Although alteration in blood flow incident to autonomic interference has been implicated by others, Taylor and Butcher found no evidence that this blood flow alteration had a regulatory influence on the eruption rate. Working with adult white rats, however, they did find that cutting the inferior alveolar nerve accelerated eruption by as much as 20 to 30 per cent over the incisor's normally innervated mate. They were then able to conclude that the influence of the dental nerve may well be due to sensory impressions conducted from the tooth and its periodontal tissue which, by reflex action, affect the use of the teeth. "Awareness of the condition of the incisor must be furnished by sensory endings around the teeth themselves, in the lips, tongue and palate, and by proprioceptive endings in the muscles of mastication."

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This experimental work, of course, is hardly at variance with common clinical experience relative to the sensibility of teeth in human beings. There is always that unique ability to detect and localize deep pressure and/or touch on the teeth or on a single tooth, a discriminatory ability which is not abolished by anesthesia. Pain is abolished by local anesthesia, but deep pressure sensibility is not. In a tooth with a root-canal filling pain is lost, but deep pressure sensibility is still felt. Attention is directed, therefore, to the responses of the teeth to various forms of sensation other than pain and to the role of a desensitized tooth as part of a wider functional whole.

A study by Lewinsky and Stewart[2] removes all doubt as to structures in the periodontal membrane (that is, receptors) which serve to mediate sensations of deep pressure. The excellent photographs published with their report show the type of sensory end organs present in the periodontal membrane of the cat. These prove to be curled-spring tension recorders similar to those which collect kinesthetic stimuli in muscles. These receptors function at both sites as specific resonators of this modality of sensation, that is, deep pressure sensibility. They supply continuous data on states of tension, be they active or passive, in the structures involved. Such receptors in the deep tissues appear to be adapted for excitation by changes going on within the organism itself.[3]

Taylor and Butcher's reference to reflex action directs attention to the actual neural arc that is fully established at the time of birth, namely, the masticatory arc, a true physiologic unit of nervous activity which provides a framework for coordinated reflex activity. In fact, such reflex activity depends upon the integrity of this arc. As early as the tenth day, lesions (artificial or otherwise) which intercept this arc at its beginning, middle, or end may well do violence to the reflex and thus limit the range of the rat's adaptation in such vital activities as sucking and, later, feeding.

OPERATION, MATERIALS AND METHODS

A search of the literature failed to yield any details concerning an operative procedure for exposure and avulsion of the inferior alveolar nerve in a 10-day-old rat weighing about 20 grams. Dissection of rats of various ages revealed that the location of the inferior alveolar foramen on the medial surface of the mandible is far from constant. Apparently, this foramen moves to a higher level as the animals age, grow, and mature. Within a given age group, however, the nerve enters the mandible at the same place. In a 10-day-old rat the foramen is close to the posterior border and at the level of a depression in the posterior border of the ramus between the angle and the condylar neck. The frequency and placement of major vessels are such that there is more chance of hemorrhage in the older rat than in those used in our study.

Another problem was that of anesthesia. When ether was used, application of the mask or cone interfered with the operative procedure. Also, these young animals did not tolerate the ether as well as do older animals. The anesthetic course was erratic and stormy, with very little margin of safety. Nembutal sodium, injected intraperitoneally, gave results that were more satisfactory

though far from normal. By trial and error, the dose for a 20 gram, 10-day-old rat was fixed at 0.20 mg. A shift of as little as 0.05 mg. sometimes spelled the difference between no effect and respiratory arrest. Nevertheless, this anesthetic left the entire operative site free for the procedure and permitted a rapid recovery. After the injection, a period of ten to twenty minutes was allowed for the drug to take effect, at the end of which time the rat was asleep. There was some reaction to painful stimuli, therefore, it was necessary to have an assistant on hand to immobilize the animal at times during the procedure. The duration of anesthesia was about forty minutes.

The question of whether or not the nursing mother would accept her offspring after operation when they were in a lethargic state presented still another problem. Trial and error proved that she would accept as many as six of these sleepy young rats in a litter of ten, as long as they exhibited some signs of movement and as long as the incisions were well sutured. Large litters of more than six fared better than smaller litters. If the mother did not accept the young rats, she would either ignore them or kill them. When she did accept them, however, her attentive care was superlative.

Details of Operative Procedure.—A 10-day-old albino rat, weighing 19 to 21 grams, was anesthetized with 0.20 mg. of Nembutal sodium injected intraperitoneally. After a period of twenty minutes the animal was asleep. With iris scissors, a vertical incision was made through skin and fascia, starting from a point 2 mm. posterior to and level with the outer canthus of the still-closed eye and extending for 5 mm. toward the angle of the mandible. After blunt dissection and mobilization of the two wound edges, retraction revealed the masseter muscle. Superiorly, the extraorbital lacrimal gland was noted. It partially obscured the facial nerve running posteroanteriorly on the surface of the masseter muscle. The parotid duct was apparent about 2 mm. below and parallel to the facial nerve. At the posterior edge of the exposed area, a large plexus of blood vessels was seen. The extraorbital lacrimal gland was mobilized and retracted out of the field, and an incision was made with a scalpel through the masseter muscle down to bone and extending between the facial nerve and parotid duct, parallel to these structures, from the posterior border of the mandible anteriorly for about 4 mm. Retraction of the masseter muscle exposed the mandible, particularly its posterior border. At this point, a notch was noted in the continuity of this border of the mandible between the angle and the condylar neck. A hooked instrument made from a No. 17 dental explorer was inserted at this notch, hook down, in an upward direction, to a depth of no more than 2 mm. An effort was made to hug the medial surface of the mandible at all times. Then the hook was swung inferiorly for 2 mm., rotated medially for about 1 mm., and withdrawn from the wound. Resistance was felt and as the hook was withdrawn, the nerve was seen as a white sinewy thread, unmistakable in appearance. At this time some hemorrhage ensued. This was controlled by pressure and absorption with cotton-tipped applicators. The nerve was now cut, avulsed, or pinched and released. If absolute alcohol was to be injected, a 1 inch 25 gauge needle was inserted for 2 mm. on the medial surface of the mandible, instead of the hook, and 0.05 c.c. was injected. The wound edges were

coapted, and the skin was held with 0000 mild chromic gut suture on an Atraumatic side-cutting eye needle. The blood was washed from the skin, and the animal was returned to its mother.

There are no other nerves in this area that even approach the inferior alveolar nerve in diameter. The latter nerve's presence upon exposure is quite definite. As for the inferior alveolar vessels, dissection of several rats failed to reveal these structures entering the foramen with the nerve. In some avulsion procedures, the nerve was removed without any significant hemorrhage. Nevertheless, histologic sections disclosed the vessels in the canal in many cases, regardless of whether or not the nerve had been avulsed.

We notched the incisor teeth in order to determine accurately their rate of eruption. The notch was made with a fine, triangular file. The rat was held on its back and immobilized by an assistant. The scruff of the neck was pulled tight, and this held the mouth open. No anesthetic was necessary. A brace, such as a cotton applicator handle, was used to hold the teeth up and the tongue out of the way. With the brace in the mouth (behind the teeth), the file was drawn across the teeth at the base of the interdental papilla; a few strokes were sufficient. This procedure caused the papilla to be torn. The wound healed, leaving a scar which served as an accurate base line for future measurements. The notches have usually grown off the teeth before the scar disappears. However, each successive notching produces its own base line. Any old scars are obliterated by the new one. Rarely does the scar disappear before the notches do.

All measurements were taken from this base line; the times of notching and measuring were known. Therefore, with the measurement, D (in millimeters), and the time, T (in days), we can calculate the rate, R (millimeter per day), by substituting the formula $R = D/T$. The rate is then expressed in millimeters of eruption per day.

Occasionally, some animals required "disking" to maintain a normal occlusal balance. The teeth may also be taken out of occlusion by this technique. The procedure is the same as that for notching, that is, holding, bracing, etc. However, a Carborundum disk is substituted for the file. The disk is used in a dental engine and run at about 3,000 r.p.m. Intermittent pressure is used, and the teeth are ground or cut to the desired length. Care must be taken to avoid exposure or laceration of the lips or tongue. Disking was not a substitute for notching, but an entirely separate procedure.

To date, twenty-five litters of young Wistar albino rats, averaging eight rats to a litter, have been used in this experimental work. All animals were raised under equal conditions of feeding and care. Animals of the same litter, experimental and control, were killed under ether anesthesia and tissues were taken as follows:

> Some mandibles were fixed in 10 per cent formalin, decalcified in 45 per cent formic acid and 6.8 per cent sodium formate, washed for twenty-four hours, and subjected to regular dehydration and embedding (paraffin). Sagittal, horizontal, and frontal sections were cut at 6 microns and stained with hematoxylin and eosin.

Other mandibles were fixed in formalin, decalcified, washed for twenty-four hours, fixed in 95 per cent alcohol with pyridine and 2 per cent silver nitrate, reduced in hydroquinone, dehydrated, and embedded in paraffin. Sections were cut at 6 microns, stained with Ranson's modification of Cajal's stain, and mounted.

Brain stems were fixed in 95 per cent alcohol and subjected to regular dehydration and embedding (paraffin). Sections were cut at 10 microns and stained with 1 per cent aqueous toluidine blue (Nissl).

Peripheral nerves (inferior alveolar nerves) were fixed in Müller's fluid, stained with 1 per cent osmic acid, dehydrated with acetone, embedded in paraffin, deparaffinized with chloroform, and mounted on chloroform base.

Experimental Animal on Day of Operation.—The albino rat, one of a litter of eight or ten, is still relatively helpless on the tenth day of its life (the day of operation in our study). It weighs about 20 grams. Its eyes are still closed, but it is well armed with the senses of touch and smell. It is just beginning to get hair. It is nursing competitively with its littermates, proof enough that its sucking reflex is well developed. Highly developed from birth are the labyrinthine proprioceptive reflexes. The young rat without sight rights itself promptly from any and all positions. It has a clumsy, waddling, broad-based gait. Within a span of two weeks the normal young animal matures rapidly. It sees on the sixteenth day and soon becomes agile, graceful, and playful.

The lower incisors, teeth of continuous eruption, appear in the oral cavity on the tenth day, quickly lengthen, and move into functional occlusion with the upper incisors six days later. It is not until the nineteenth day of life that the first molars appear[4]; they are in occlusion by the twenty-fifth day. Given these facilities for cutting, tearing, gnawing, and grinding, it is no accident that normal young animals leave their mothers in this interval between the nineteenth and the twenty-fifth days and begin to feed on their own. From this point on, the normal experimental rat seeks and eats the pellet diet and at the same time is able to detect and avoid injurious stresses on these new signalizers of its external and internal environment.

INNERVATION

The inferior alveolar nerve is a slender white cord, even in the 10-day-old rat. It enters the mandible through a foramen in the ramus and is at once protected, as are all other parts of the nervous system, by encasing bone. The nerve traverses a bony canal which is well defined, on section, between the lingual margins of the incisor and the roots of the molars (Fig. 1). Even though many branches are given off from the main trunk as it courses through the canal, there is still a substantial residuum when it leaves the canal through the mental foramen to become the mental nerve.

The distribution of the inferior alveolar nerve to dental structures, that is, the periodontal membrane, the gingiva, and the pulp, has been the subject of a

number of excellent studies. One of the more recent[5] of these studies traces one set of fibers from a first branch, the common dental nerve, through the apical alveolar plate. On dividing, this set of fibers supplies each surface of the periodontal membrane surrounding the tooth. A second set, perforating branches of the interalveolar nerves, ascends through the bone and pierces the cribriform plate at various levels to unite with the first set of fibers. The common bundle then proceeds through the membrane toward the gingiva. As for the pulp, bundles of the first set of fibers (but of far smaller caliber) unite around the apical foramen to form the common pulpal nerve. This branch arborizes in the coronal part of the pulp.

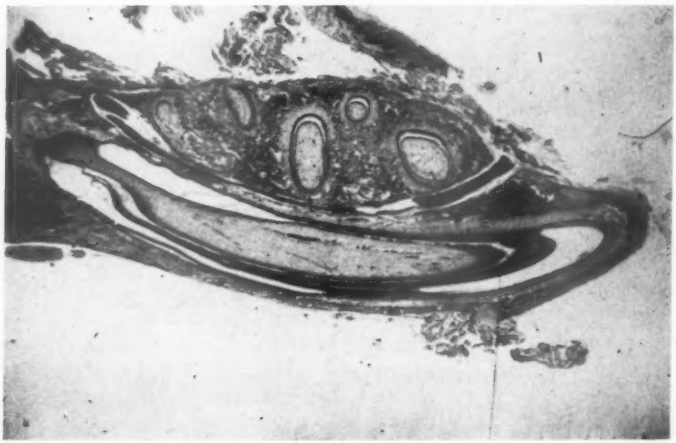

Fig. 1.—Inferior alveolar nerve in mandible of young normal animal from point of entry to point of exit.

That such facilities not only exist in the white rat but are fully developed at the time of birth is shown by a photomicrograph of the incisor and its environs in a newborn (Fig. 2). In a frontal section of the mandible of a rat killed on the second day of life a large fascicle of this nerve is seen dividing and subsequently supplying fibers to all surfaces of the periodontal membrane surrounding the tooth. Longitudinal and cross-section views, taken later, of the main trunk of the inferior alveolar nerve in the mandibular canal clearly show a preponderance of large and medium-sized myelinated fibers (Fig. 3). A large majority of fibers in fascicles from the main nerve are likewise myelinated and retain their sheaths until close to their termination in the membrane (Fig. 4).

Even smaller branches (that is, perforating fibers of the interalveolar nerve) are still myelinated when they pierce the cribriform plate to join those fibers in the periodontal membrane coming from the apex of the tooth. Reference has already been made to spindlelike structures in the membrane, that is, terminations of these fibers. Pulpal fibers which enter the apical foramen are, in contrast, of much smaller caliber. Windle,[6] reporting on an investigation of the

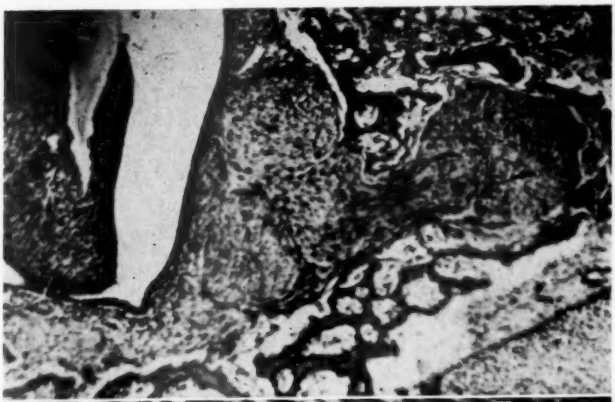

Fig. 2.

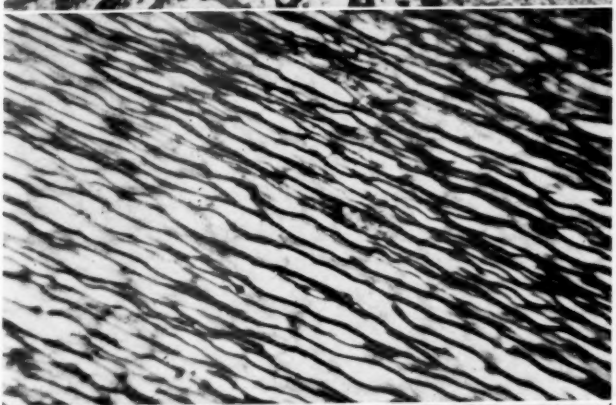

Fig. 3.

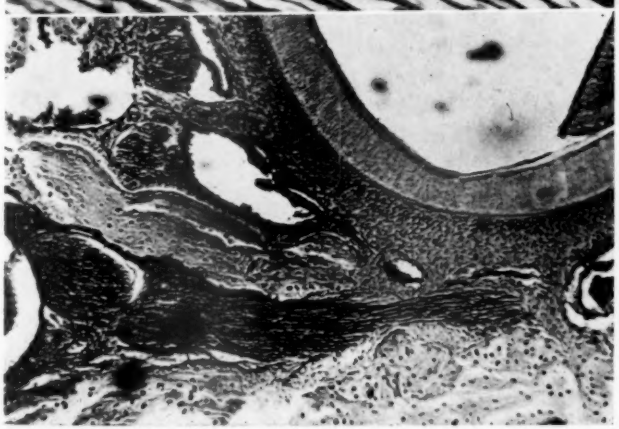

Fig. 4.

Fig. 2.—Inferior alveolar nerve in 2-day-old normal animal. Note branching of large fascicle to supply periodontal membrane.

Fig. 3.—Longitudinal view of large and medium myelinated fibers in inferior alveolar nerve.

Fig. 4.—Nerve after its division, showing type and size of fibers in branches to periodontal membrane.

innervation of the tooth pulp, states: "Since no large myelinated fibers and few myelinated fibers pass into the pulp cavity these large myelinated fibers must belong to nerves or fibers innervating the periodontal membrane." Ranson's[8] extensive work proved that pain is conveyed by nonmedullated or finely medullated fibers. It follows, then, that the large and medium-sized medullated fibers subserve the modality of deep pressure proprioception in the periodontal membrane.

EXPERIMENT

Objectives.—The anatomic and functional integrity of a nerve fiber is preserved only if the fiber is in continuity with its parent cell body. If a nerve fiber is cut off from its cell of origin, it degenerates. It follows, therefore, that local surgical severance of the inferior alveolar nerve at the site of its entrance into the mandibular canal will be followed by degeneration in fibers of the distal segment, a degeneration that requires days for completion. Proof of this degeneration can be obtained with preparations stained specifically with osmic acid.

When a nerve fiber is cut, parts of the neuron central to the severance show characteristic changes also. The fiber's parent cell body undergoes reactionary chromatolysis. This change is essentially one of solution and redistribution of the Nissl substance and of changes in the position of the nucleus. This, too, can be demonstrated with appropriate stains of the cell body.

Surgical severance of the sensory inferior alveolar nerve branch of the mandibular nerve causes a lesion which constricts the field of reception in the structures served by this nerve. Receptors in this field subserve deep pressure proprioception, and the signals entering this path to the center are essentially kinesthetic stimuli. Along the sensory path of this neural arc the normal animal is warned against and prepared for changes in its internal and external environment that are approaching in space and time. Thus warned and prepared, the animal responds appropriately.

One of the immediate objectives of the operations performed in our study was to measure and record actual changes in the eruption rate (that is, a functional rate) of the mandibular incisor after nerve severance. It was believed that this operation, together with another form of transient interference (nerve crushing or compression), would lead to a more complete understanding of the actual mechanism involved in the nervous control of the rate of eruption.

Results of Nerve-Severance Operations.—

Unilateral inferior alveolar nerve severance, with or without avulsion: Following transection of the nerve on one side, the incisor tooth on that side invariably exhibited an acceleration of eruption. Visual evidence of this acceleration began to appear within a week or ten days after denervation. Not infrequently, this tooth and its normal mate became unequal in length; the desensitized tooth was slightly longer. When it grew too long, it occasionally fractured and, as a result, became shorter. However, this tooth soon caught up with its mate. In the interval, various distortions of occlusion were common and were often corrected. Nothing like this happened in the control animals. The incisor on the

nerve-severed side also differed from its mate by exhibiting a loss of pigment. The tooth became porcelain white, and this loss of pigment persisted. Teeth in the control animal were normally pigmented and stayed that way. The teeth were notched to give an accurate record of the eruption rate. Notching was not

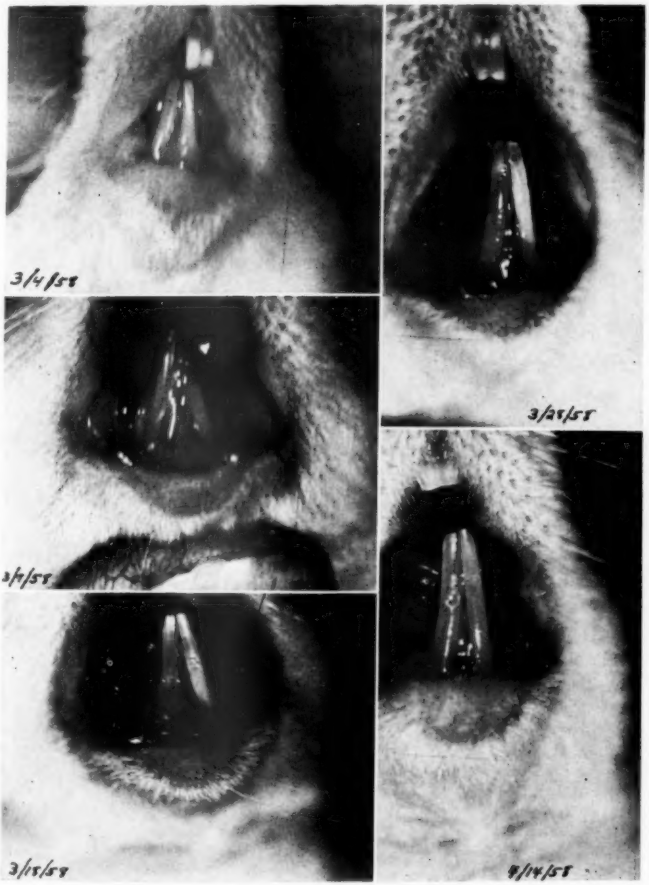

Fig. 5.—Animal A of litter XI, with inferior alveolar nerve severed unilaterally, photographed before and after notching on successive days.

attempted before the twenty-fifth to the thirtieth day in order to ensure degeneration in fibers of the distal segment of the nerve. With notches on the teeth, the actual rate of eruption was determined by measuring, at regular intervals, the distance from a scar at the gingival crest to the notch on the labial surface of the tooth (Figs. 5 and 6). Both lower incisors in animal A of litter VI were first notched on the thirty-second day of the animal's life. They were notched periodically thereafter whenever the existing notches had disappeared. The rate

of eruption over sixty-nine days was 1.15 mm. per day for the denervated tooth (left), in contrast to a rate of 0.78 mm. in the normal tooth (right). This represented a 29 per cent increase in the eruption rate of the denervated tooth over its mate. The acceleration persisted until the animal was killed on the

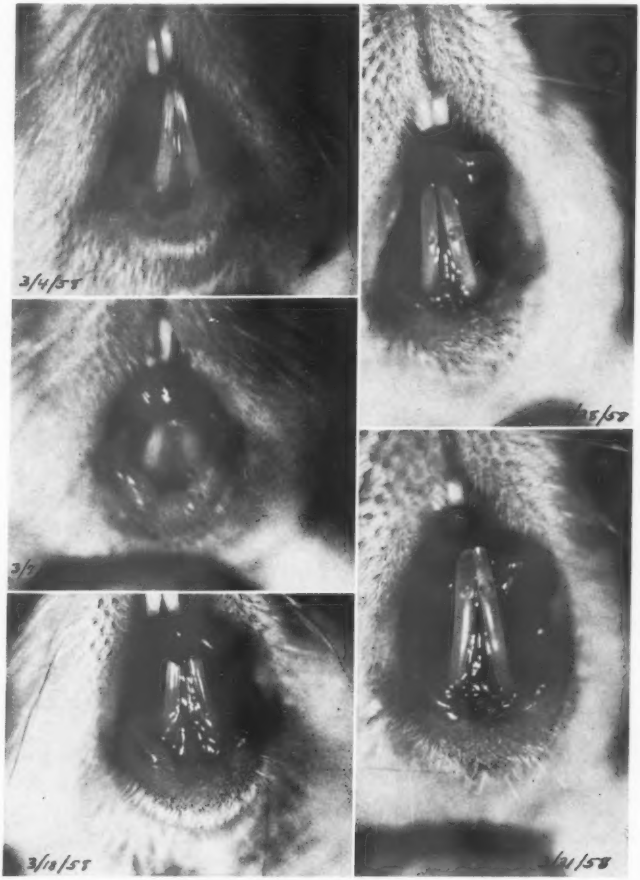

Fig. 6.—Animal D of litter XI, with inferior alveolar nerve severed bilaterally, photographed before and after notching on successive days.

sixty-ninth day. The denervated tooth contrasted sharply with its mate in pigmentation. It turned porcelain white and remained so until the animal was killed. The normal tooth was normally pigmented from the beginning to the end of the run. Early in this run the denervated tooth fractured at its distal tip, and for several days it was actually shorter than its mate. Within three or four days, however, it caught up and both teeth were again in functional occlusion with the upper teeth.

In rat C of the same litter, the rate of eruption over sixty-seven days was 0.88 mm. per day in the denervated tooth and 0.66 mm. per day in the normally innervated tooth. Thus, the surgical intervention produced an acceleration of 25 per cent. The denervated tooth lost pigment, became porcelain white, and

Fig. 7.—Degenerated fragment of nerve in the canal of an animal whose inferior alveolar nerve was transected on one side.

remained that way until the rat was killed on the sixty-seventh day. The involved tooth in this rat also fractured at its tip early in the course of the experiment. It rapidly regained length, however, and within three days was in functional occlusion with the upper teeth.

There were two controls (F and G) in litter VI. In both animals the lower incisors were periodically notched. The notches were invariably equidistant from the gingival scars at the bases of both teeth. There was no acceleration in rate of eruption. In fact, the rate in both teeth averaged that of the innervated tooth in the animals that were operated on. There was no loss of pigment at any time. There were no fractures. (Indeed, throughout the entire series there were no fractures among the control animals; nor were there any fractures in the innervated teeth of the animals subjected to surgical intervention.)

Animals in this as in all other litters were raised under equal conditions of feeding and care. There were no fluctuations in the environment. In spite of this, several animals with unilaterally and bilaterally denervated teeth died of starvation. They survived the operation but lost weight continuously and thus were unable to compete successfully with their littermates for food, either liquid or solid. Furthermore, animals A and C of litter VI weighed 126 grams and 129 grams, respectively, on the fifty-fifth day of their lives (they were killed on the sixty-seventh day) as compared 167 grams in control animal F of the same litter. This loss of weight or failure to gain weight became a commonplace, a monotonous result of the specific operation of nerve severance. That it had little

TABLE I. ERUPTION RATES AND CHANGES IN PIGMENT IN A SERIES OF THREE LITTERS*

ANIMAL	PROCEDURE	RATE OF ERUPTION OF MANDIBULAR INCISOR (MM./DAY)		INCREASE IN RATE OF ERUPTION OF DENERVATED TOOTH OVER ITS CONTROL (PER CENT)	PIGMENT		WEIGHT AT DEATH (GRAMS)	AGE AT DEATH (DAYS)
		LEFT	RIGHT		LEFT	RIGHT		
				Litter V				
C	Unilateral severance	1.13	0.88	22	Porcelain	Normal		57
G	Control	0.92	0.92		Normal	Normal		57
H	Control	0.92	0.92		Normal	Normal		67
				Litter VI				
A	Unilateral severance	1.1	0.78	29	Porcelain	Normal		69
C	Unilateral severance	0.88	0.66	25	Porcelain	Normal		67
F	Control	0.70	0.70		Normal	Normal		67
G	Control	0.72	0.72		Normal	Normal		67
				Litter VII				
D	Operation, no severance	0.60	0.59		Normal	Normal	157	58
E	Control	0.69	0.69		Normal	Normal	186	58

*Animals operated upon without nerve severance are included.

O.S., O.M. & O.P.
October, 1951

to do with the trauma of the operation itself was proved by the rapid gains in weight of animals subjected to the operation but without nerve severance (Table 1, animal D of litter VII).

Histologic sections of the mandibles of these rats at the time of death (sixty-seventh day) were revealing. The nerve trunk (inferior alveolar nerve) was well visualized in the canals of all control animals. It was well defined on the nonsevered side (right) of the animals subjected to surgical nerve severance, but it had either degenerated or was missing altogether from the side of severance (left) in the same animals (Fig. 7). Both results were taken as indices of a successful operation. Additional proof of degeneration in the nerve was provided by osmic acid stains of the peripheral segment. Here the degenerated myelin was in the form of a black powdered deposit along the course of the afferent fibers.

In notching the teeth, we found a zonal loss of pigment—a white zone—at the site of notching, which was comparable in quality to the total loss following nerve severance. Here it was obvious that we had deliberately reduced the thickness of the calcified substance on the teeth locally. We believed that histologic sections might provide some clue as to the reasons for loss of pigment in the nerve-severed teeth. As visual evidence in our sections, we found a sharp contrast between the thickness of enamel and dentine in the nerve-severed incisor and its innervated mate in the same animal. In fact, the calcified layers in the tooth were sometimes only one-half as thick on the severed side (Fig. 8).

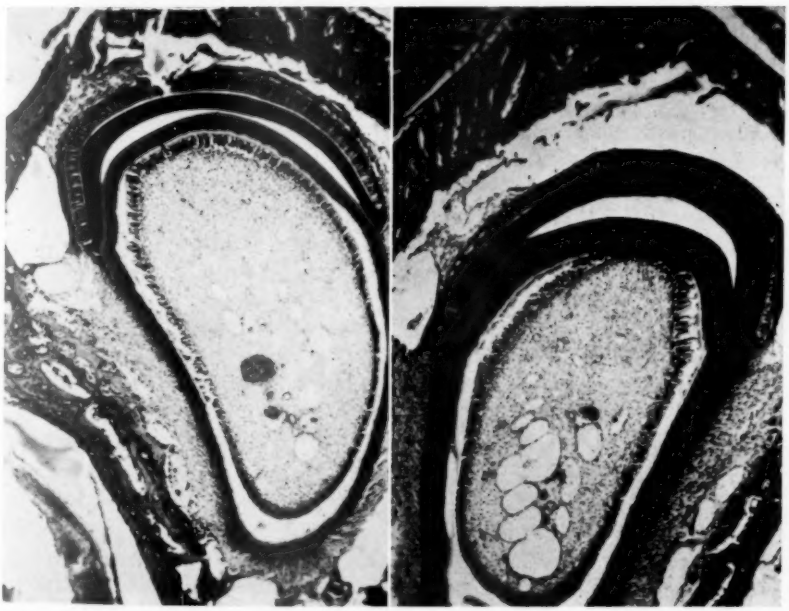

Fig. 8.—Contrast between the depths of enamel and dentine in nerve-severed and innervated incisors in the same animal.

TABLE II. EXPERIMENTAL RUN OF ANIMALS IN A SINGLE LITTER (VIII) SUBJECTED TO EITHER INFERIOR ALVEOLAR NERVE TRANSECTION (ONE OR BOTH SIDES), NERVE CRUSHING, OR MENTAL NERVE SEVERANCE

ANIMAL	PROCEDURE	RATE OF ERUPTION OF MANDIBULAR INCISORS (MM./DAY)		INCREASE IN RATE OF ERUPTION OF DENERVATED TOOTH OVER ITS CONTROL (PER CENT)	PIGMENT		WEIGHT AT DEATH (GRAMS)	AGE AT DEATH (DAYS)
		LEFT	RIGHT		LEFT	RIGHT		
B	Bilateral severance	0.71	0.72	38 (over control animal)*	Depigmented (leopard spotting)	Depigmented (leopard spotting)	138.0	114
C	Left mental nerve severance	0.47	0.47		Normal	Normal	145.0	56
D	Bilateral mental nerve severance	0.55	0.55		Normal	Normal	114.0	56
F	Unilateral severance	0.73	0.52	29	Porcelain	Normal	215.0	69
G	Unilateral pinching	0.59	0.48	19	Lost and re-gained pigment	Normal	185.0	114
H	Control	0.45	0.44		Normal	Normal	162.0	56
I	Control	0.48	0.48		Normal	Normal	172.0	67

*This animal had a bilateral operation and is therefore compared with the average rate of several control animals.

O.S., O.M. & O.P.
October, 1941

Taylor and Butcher[1] found the same thing when they relieved the rat's incisor of functional pressure, that is, when they took it out of occlusion. The acceleration in eruption under these conditions reduced the time necessary for full appositional growth of dentine and enamel. In accelerating the rate, nerve severance also reduces the time for appositional growth and thus the time necessary for pigment deposition on the tooth. The end result in either case, therefore is a true dissociation between the growth of tooth substance and the rate of eruption of the tooth.

Mental Nerve Severance: The mental nerve was severed on one side in animal C and on both sides in animal D of litter VIII. The rates of eruption were recorded for an extended period following these operations. This procedure had no effect upon the eruption rate of one or both teeth. Eruption of these teeth was not accelerated beyond that of the teeth of the control animals. In both animals the teeth were normally pigmented throughout the course of the experiment.

Bilateral Nerve Severance: In this same series the inferior alveolar nerves were severed bilaterally for the first time in animal B of litter VIII (Table II). The eruption rates of both teeth were approximately equal. Both teeth, however, showed an acceleration of 38 per cent beyond the rate in the control animals of the same litter. Both nerves were cut, of course, to study the rate of eruption and pigmentary changes in teeth so treated. Bilateral nerve severance was viewed as a further invasion of structures linked in functional unity and therefore was thought likely to produce a greater functional deficit than nerve severance on one side only. Such an operation could well lead to a more serious restriction in the range of the animal's activity and further disturb its equilibrium with its surroundings.

Both teeth in rat B fractured early and then fractured again in the middle of the experiment. Both teeth grew in rapidly—so rapidly, in fact, that disking was required in order to keep them in some kind of occlusion. This disking was done on three or four occasions. In the last few days of the animal's life, the right tooth fractured for the third time. Both teeth became depigmented and then regained some pigment, but both teeth were leopard spotted when the animal was killed at the age of 114 days. This animal ran a stormy course. Its weight was only 138 grams at the time of death. Its littermate, a pinched animal, weighed 185 grams at 114 days. At 56 days its control littermate weighed 162 grams. Another control weighed 172 grams at 67 days. Animal B weighed only 104 grams at 69 days.

Crushing: Nerve crushing or compression involves the lifting of the nerve from its bed, pinching it with a watchmaker's forceps, and then returning it to its bed. In essence, this procedure is a form of transient interference with conduction along the afferent arm of the neural arc. The objective, of course, was to measure the rate of eruption and to record changes in pigmentation in the tooth under these conditions. In contrast to the effects of conduction anesthesia, large and medium-sized myelinated fibers which subserve deep pressure sensibility are first "to go" when these fibers are pinched or compressed.

In what might be called a "short-term pinched series," the left inferior alveolar nerve in animal A of litter VII was crushed on the tenth day of life. Both teeth were of equal length and of the same color until the twenty-fifth day, when color changes were recorded on the left incisor. On the twenty-ninth day, the tooth was described as porcelain white. It remained porcelain white until the animal was killed on the fifty-eighth day. In addition, on the twenty-ninth day this tooth became slightly longer than its mate and it fractured on the thirtieth day. By the fortieth day it had regained its length, it was equal to its mate, and it was in occlusion with the upper teeth. Thereafter, the notches were no longer even on both teeth, indicating a differential rate of eruption. The actual rate of eruption for the two teeth was 0.82 mm. per day for the left and 0.72 mm. per day for the right—a 12 per cent increase in the left over the right.

Because of the acceleration in the rate of eruption of the involved tooth (L) and the pigment loss which this tooth sustained until the end, it was difficult to distinguish the result of the crushing procedure from that of actual nerve severance. The acceleration in rate, however, was only 12 per cent, about one-half the average acceleration produced by nerve severance. The loss of pigment on the tooth persisted. These results were interpreted as follows: The nerve was crush-pinched, but the time which elapsed between crushing and the animal's death (forty-eight days) was insufficient for full recovery. To get a functionally reversible result, one would have to kill the animal at a later date. A short-term pinched series does not allow for this.

The left inferior alvolar nerve was pinch-crushed in animal B of litter VII. In this rat the rates of eruption of the two teeth were essentially the same—0.743 mm. (left) and 0.741 mm. (right) per day. There was no acceleration of eruption, and no difference in pigmentation on the two teeth was seen until the forty-sixth day, when the left tooth was described as "lighter." Actual porcelain-white changes in this tooth were described between the forty-eighth and fifty-fifth days. On the day of the animal's death (fifty-eighth day), however, there was no great difference in pigment between the left tooth and the right tooth. In this case, with no change in rate and only the slightest change in pigment, it is debatable whether actual crushing had been accomplished. This might well be classified as an "unsuccessful crush."

In another run in what was called the "long-term pinched series," the left inferior alveolar nerve was crushed or pinched in animal G of litter VIII (Table II). In this rat, which was killed on the 114th day, the long-term increase in the rate of eruption of the left over the right tooth was 19 per cent (0.59 mm. per day for the left and 0.48 mm. per day for the right). The tooth lost pigment and became porcelain white from the fortieth to the fifty-sixth days. Thereafter, although there was a contrast in pigmentation in the two teeth, this was never extreme. By the seventy-sixth day the tooth had regained its pigment and never lost it again until the animal was killed on the 114th day. Over the whole of the latter interval (days 76 to 114) the two teeth were described as normally pigmented. In this case, with an acceleration of 19 per cent in the eruption rate and a transient loss and then return of pigment in the involved

tooth, it is hardly debatable that a true crush was obtained. It follows also that the changes in nerve conduction which took place were reversible and not like those degenerative changes which follow severance. Finally, this rat weighed only 125 grams on the fifty-sixth day of its life. This contrasted sharply with its control littermate which weighed 162 grams on the fifty-sixth day. From this day on, however, the pinched rat gained weight steadily until it was killed at 114 days, at which time it weighed 185 grams.

Ground-Pellet Diet.—Conditions of feeding were deliberately changed in animals of litter XIII. With the straight hard-pellet diet, we had lost several animals with unilaterally and bilaterally severed inferior alveolar nerves. Failure to make consistent gains in weight was sometimes marked among the animals that had been operated on, particularly those that had undergone bilateral severance. To save animals, to reduce the incidence of fracture to a minimum, and to record changes in the eruption rate under conditions of changed diet, we gave the animals in litter XIII a ground-pellet diet. Hard pellets were put through a meat grinder, and the resulting coarse, ground meal was fed to all animals in this litter.

The inferior alveolar nerves were severed bilaterally in rats A, C, and E of litter XIII on the tenth day of their lives. The teeth were notched for the first time on the fortieth day and periodically thereafter until the animals were killed on the eighty-fifth day. The eruption rates in these animals were 29.4 per cent (animal A), 13.5 per cent (animal C), and 17.2 per cent (animal E) higher than in the control animals. There was a common denominator, however; eruption rates, although increased over the rates in the control animals, were considerably lower than the rates in animals of the experimental group raised on a hard-pellet diet. Although bilateral fractures of the incisors occurred in animals C and E on the thirtieth day of life, both teeth had grown out and were in functional occlusion with the upper incisors at the time of the first notching on the fortieth day. No fractures occurred thereafter. The teeth in animal A of litter XIII remained unfractured throughout the course of the experiment. These animals gained weight easily and sustained these gains throughout their lives.

In contrast to the normal pigmentation in the teeth of the controls, the teeth in these rats with bilaterally sectioned inferior alveolar nerves were uniformly lighter in color and often translucent. They never became porcelain white, as did the teeth in animals of other litters raised on the hard-pellet diet.

Animal B of litter XIII underwent an operation on one side. The eruption rates on both sides were approximately equal—0.54 mm. per day on the left and 0.53 mm. per day on the right. The left tooth was lighter than the right one throughout this run. In this case, with no differential in rate and only shade differences in pigmentation, it is debatable whether nerve severance was actually accomplished.

A control animal in litter XIII was used to study changes in the rate of eruption when the incisors were taken out of occlusion by disking. Both teeth were periodically disked and notched from the forty-second day to the eighty-

TABLE III. ERUPTION RATES AND CHANGES IN PIGMENT AMONG DENERVATED ANIMALS AND THEIR CONTROLS RAISED ON A GROUND-PELLET DIET*

ANIMAL	PROCEDURE	RATE OF ERUPTION OF MANDIBULAR INCISORS (MM./DAY)		INCREASE IN RATE OF ERUPTION OF DENERVATED TOOTH OVER ITS CONTROL (PER CENT)	PIGMENT		WEIGHT AT DEATH (GRAMS)	AGE AT DEATH (DAYS)
		LEFT	RIGHT		LEFT	RIGHT		
A	Bilateral severance	0.67	0.69	29.4 (over control animal)†	Light and translucent	Light and translucent	335	85
B	Unilateral severance	0.54	0.53		Light	Normal	284	85
C	Bilateral severance	0.55	0.56	13.5 (over control animal)†	Light and translucent	Light and translucent	220	85
E	Bilateral severance	0.58	0.58	17.2 (over control animal)†	Light and translucent	Light and translucent	316	85
Control	Red tail	0.52‡	0.46		Normal	Normal	221	85
Control	Disked	0.72	0.72	33.3§	Lighter than normal	Lighter than normal	356	85

*All animals of litter XIII were kept on a ground-pellet diet.
†This animal had a bilateral operation and is therefore compared with the average rate of several control animals.
‡This animal fractured its left incisor at the notch; therefore, the rate of eruption of this tooth increased over that of its mate.
§Increase over average control rate.

fifth day, when the animal was killed. There was an immediate response, with both teeth showing an equal acceleration in eruption of 33 per cent over the normal control rate. Thus, since occlusal stress was constantly eliminated, this new rate persisted until the animal was killed on the eighty-fifth day. The closeness of this rate to the rate of acceleration in bilaterally sectioned animals in this and other litters was striking. Finally, both teeth became lighter than normal in color and remained that way until the experiment was terminated on the eighty-fifth day.

Experience gained during the course of this experimental work led us to alter somewhat the time sequences for notching and for measuring and recording the eruption rate. Because of the thinness and fragility of the newly erupted teeth in these young animals, we found it hazardous to attempt to notch teeth in the early days following the operation. Notching before the thirty-fifth to the fortieth day merely invited fracture (that is, breaking of a tooth or teeth at the notch). Notching after the fortieth day carried with it none of these hazards. We learned, therefore, to wait until the teeth were stabilized around the fortieth day before beginning to notch. In addition, we learned during an experimental run to wait until the notches were disappearing from the teeth before renotching; thus, we avoided inflicting a needless load on young teeth. With these precautions, fractures were reduced to a minimum or were prevented altogether. As a result, our measured and recorded eruption rates and pigmentary changes were calculated only on nonfractured teeth.

Reference is made here to animals A, C, and E of litter XIII, all of which underwent bilateral nerve severance. Notching in these animals began on the fortieth day. From that day until the animals were killed, there were no fractures. The accelerations in rate and the pigmentary changes are listed in Table III.

In animal D of litter XVI and in animal D of litter XVII, two unilaterally nerve-severed animals, no fractures occurred after notching began about the fortieth day. Measured rates, therefore, were on unfractured teeth.

In two animals (D and E of litter XX) with unilaterally severed nerves, the teeth never fractured after notching began. The measured and recorded rates, therefore, were rates uncomplicated by fracture.

In animal C of litter XXI, a unilaterally nerve-severed animal, the tooth was unfractured from beginning to end. In animal D of the same litter, the involved teeth remained unfractured after notching began on the fortieth day.

Mesencephalic Nucleus and Root of Fifth Cranial Nerve.—Discussion thus far has centered around the centripetal third of the neural arc. At this point attention is directed to the subcortical, segmental center of the arc—the middle third. Where, in the neural axis, are the cells of origin, the nuclear center of the large and medium-sized myelinated fibers in the inferior alveolar nerve? What happens to the cells in this nucleus when the centripetal nerve is cut? Are these changes demonstrable? How reliable is Nissl granule degeneration as an index of neuron injury? Have other methods been used to demonstrate the relationship between cells in the nucleus and fibers at the periphery?

The position of the mesencephalic nucleus of the trigeminal nerve in the alar plate indicates that it is a sensory nucleus. The close resemblance of its cells to cells of a spinal ganglion again marks it not only as sensory but as the only group of ganglion cells which have moved into the neural axis, all others remaining outside.

Prior to Corbin's[11] careful studies of the peripheral distribution of fibers rising in the mesencephalic nucleus of the trigeminal nerve, few workers even suggested that the mesencephalic nucleus contributed to nerves other than the motor fifth. Johnston[9] and Kosaka[10] were notable exceptions.

Corbin used the Horsley-Clarke instrument to destroy cells in the mesencephalic nucleus in the cat.[11] Following unilateral destruction of the mesencephalic nucleus and root at caudal and higher levels he found, with osmic acid techniques, that degeneration in large and medium-sized myelinated fibers could be traced peripherally into the following divisions of the fifth cranial nerve on the same side: (1) the superior alveolar branch of the maxillary division; (2) the branches of the mandibular division among the muscles of mastication and finally the inferior alveolar nerve branch of the mandibular division of the fifth cranial nerve. The other branches of the fifth nerve were free of degeneration. Fiber degeneration did not extend into the mental nerve. In no case were fibers from the mesencephalic nucleus found entering the contralateral branches of the fifth cranial nerve. Corbin thus demonstrated, perhaps for the first time, that mesencephalic nucleus root fibers passed peripherally not only into the masticatory branches of the fifth cranial nerve but also into the purely sensory branches, that is, the superior alveolar, palatine, and inferior alveolar nerves which supply deep pressure sensibility to the teeth, periodontal membranes, gingivae, and hard palate.

In a second series of experiments on the cat, Corbin and Harrison,[12] using an insulated nichrome wire as one lead and the Horsley-Clarke instrument as the other, obtained striking action potentials from the mesencephalic nucleus root in response to such physiologic stimuli as jaw opening. Extension of the masticatory muscles by gravity alone evoked an excellent response. Such responses were obtained by pressing on the homolateral masticatory muscles. In addition, blunt pressure stimulation of the lower and upper teeth of the homolateral jaw (especially of the canines) and finally of the hard palate resulted in a marked increase in the height and frequency of action potentials obtained from the caudal half of the mesencephalic nucleus root. All this was in complete conformity with proprioceptive action potentials obtained elsewhere. "Except for this response resulting from jaw opening and blunt pressure stimulation of the teeth, gums, and hard palate, there were no responses from the mesencephalic nucleus root when other structures from the head and buccal regions were stimulated."

In this series of careful experiments Corbin and Harrison (1) demonstrated the actual peripheral distribution of fibers which have their origin in the mesencephalic nucleus and root of the trigeminal nerve and (2) correlated electrical responses in this nucleus to the stimulation of peripheral receptors having specific

sites and specific properties. Both steps were necessary to prove the existence of a highly stable anatomic substratum for segmental reflex activity at this level, a substratum which was functionally demonstrable.

The specific receptors in this stable substratum are located in the supporting structures of the teeth, that is, in the periodontal membranes, in the hard palate, and in the muscles of mastication. Large and medium-sized medullated fibers which have their origin in the mesencephalic nucleus and terminate in these receptors, mediate proprioceptive impulses from the muscles of mastication and deep pressure from the teeth, their supporting structures, the gingivae, and the hard palate. These fibers and this nucleus may be considered as forming the afferent limb of the masticatory reflex arc—its centripetal third. Cajal[13] has demonstrated central collaterals (intersegmental connections) passing from the mesencephalic nucleus to the motor fifth nerve. These and other segmental association neurons constitute the middle third of the arc. Fibers which form the efferent limb of the arc (its centrifugal third) take origin from the multipolar cells of the motor fifth nerve. These fibers make up the peripheral nerve and its branches which pass to terminal effectors in the muscles of mastication.

In his first article Corbin[11] refers to the earlier works of Pfaffmann and Sherrington. Pfaffmann[14] obtained action potentials from the superior alveolar nerve after pressure was applied to the teeth, the gingivae, and even the adjacent lips. The fact that these impulses were slowly adapting and were rapidly conducted implied that they were mediated by large myelinated fibers. Pfaffmann removed the dental pulp and destroyed the nerves in the apical canal and still got a maximum response. Here was evidence which indicated that the majority of endings giving rise to these impulses were located in the periodontal membranes and not in the mucosa or in the pulp. Superficial mucosal endings are terminals of fibers that have their cells of origin in the Gasserian ganglion and are concerned with exteroceptive sensation (light touch, pain, and temperature). Endings in the pulp are terminals of fibers that also have cells of origin in the Gasserian ganglion and subserve sensations of pain and temperature. Sherrington[15] applied blunt pressure as a stimulus to the gingivae bordering the teeth of both upper and lower jaws, to the tooth crowns, and to the hard palate. He obtained reflex opening of the tonically closed jaw in the decerebrate animal (cat). This involved both a reflex inhibition of the jaw-closing muscles and a concurrent stimulation of the jaw-opening muscles. It would be hard to conceive of a more striking exhibition of reciprocal innervation with its inhibition of antagonistic antigravity muscles.

Here, then, was almost irrefutable evidence, anatomic and physiologic, regarding the function of the mesencephalic nucleus and root, a vital link in the masticatory reflex arc. Corbin and Harrison[12] could thus conclude:

> The mesencephalic nucleus may well be considered the cells of origin of the afferent fibers concerned in the reflex control of mastication; the pressure sensations elicited from the deeper tissues of the jaw would then serve to control the force of the bite, preventing damage to the teeth, gums and palate. Impulses arising from the teeth (periodontal membranes), gums and palate would then not only inhibit activity of the jaw closers through inhibition of the motor nucleus of the Vth and thus inhibition of the activity of the muscles of mastication, but also

actively elicit jaw opening through reflex stimulation of the motor nerves supplying the mandibular depressors. The latter action would be partially mediated through the motor nucleus of the Vth supplying the mylohyoid and anterior belly of the digastric.

Thus, impulses mediated by the fibers just described, together with those passing over the masticatory nerves from the muscles of mastication, make up the afferent limb of the masticatory reflex arcs and thereby coordinate and control chewing movements. Also enlightening in this respect are the earlier studies of Berkelbach van der Sprenkel,[16] who described "end rings" in the periodontal membrane which, he concluded, served as pressure receptors regulating "chewing pressure."

EXPERIMENTAL RESULTS

All studies have shown that the mesencephalic nucleus root of the fifth cranial nerve is a constant formation in vertebrates.[17-19] In higher mammals, including the rat, the nucleus of the mesencephalic nucleus root of the fifth cranial nerve extends from the midbrain into the region of the pons to the level of the motor root of the fifth nerve. The nucleus is a paired column of cells which appears on both sides of the brain stem and extends in a longitudinal direction for a distance of about 3.25 mm. The cells gather in small clusters lateral to the aqueduct in the midbrain and just lateral to the fourth ventricle in the pons.

In the rat only a few cells appear at the rostral end of the midbrain, but toward the caudal end the number of cells increases. From the level of the trochlear nucleus, the number of cells increases to twenty or thirty. In the rat, therefore, there is a conspicuous concentration of cells in the caudal half of the mesencephalic nucleus. This concentration is even more pronounced as one approaches the nucleus of the motor root of the trigeminal nerve.

The cells in this nucleus are round to oval to pear-shaped. On the whole, they are large to medium in size (15 to 30 microns). They are unipolar, in sharp contrast to the multipolar cells in the nucleus of the motor root of the fifth cranial nerve. The nuclei in these cells are large and spherical. These nuclei stain lightly and are often almost transparent. They carry a centrally placed dark-staining nucleolus. In normal cells the tigroid or Nissl substance is well differentiated and equally distributed through the whole cell body.

What happens, then, to the cells of this nucleus when the centripetal path is severed? Certainly, no changes could be expected unless the animal is permitted to live at least three weeks in order to ensure ample time for such changes to occur. Does reactionary chromatolysis take place in the cell bodies of origin of the cut fibers? Are these changes characteristic? It might be added that the time of the peak reaction after injury would vary somewhat with the distance of the injury from the cell. Before we cite experimental results, it is essential to emphasize that the cell population of this nucleus is heterogeneous. The mesencephalic nucleus receives deep sensibility fibers not only from the muscles of mastication but also from purely sensory branches of the fifth cranial nerve (that is, the superior alveolar, palatine, and inferior alveolar nerves). It is obvious that retrograde degeneration could not be expected in cells of this nucleus which

Fig. 9.

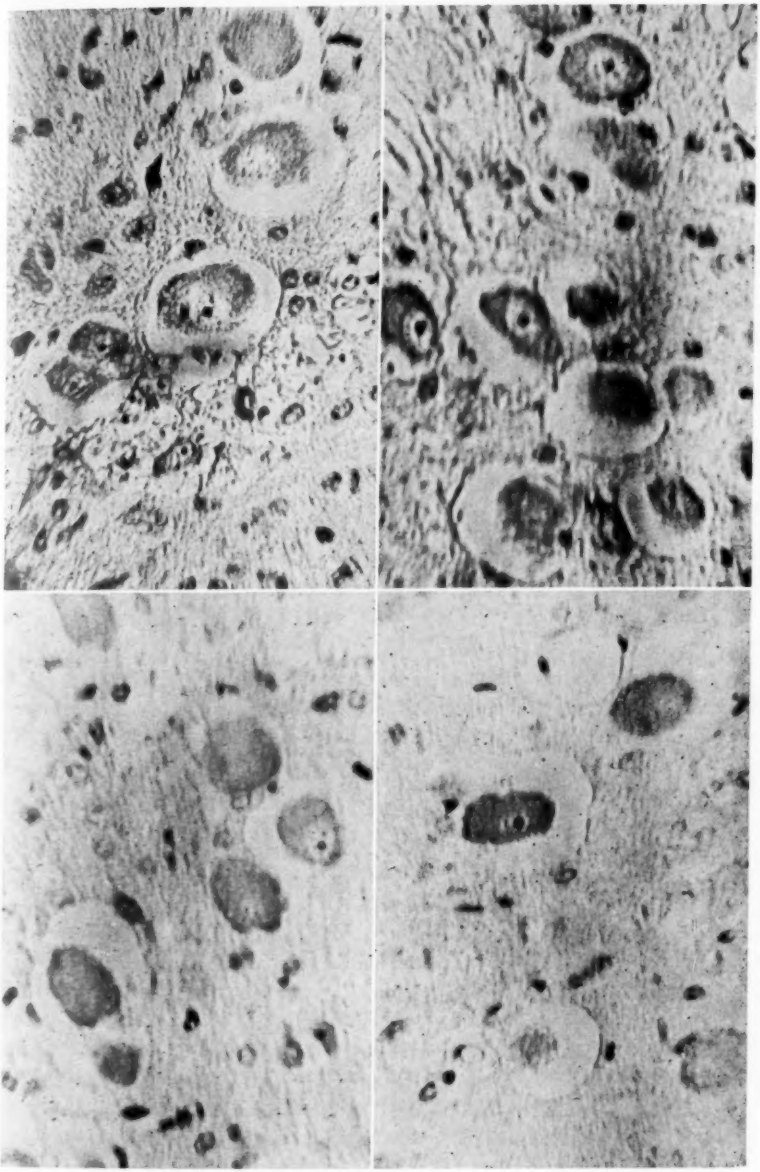

Fig. 10.

Fig. 9.—Mesencephalic nucleus. Note paired column of cells at a caudal pontine level in control animal E of litter XXIII. (Nissl preparation.)

Fig. 10.—Mesencephalic nucleus on both sides at same level in animal A of litter XXIII with inferior alveolar nerve severed bilaterally. (Nissl preparation.)

receive fibers from the muscles of mastication or from structures in the upper jaw. These fibers are not interrupted; as a result, their cells of origin are unscathed by severance. It is only in cells of the nucleus which receive fibers from the inferior alveolar nerve that reactionary chromatolytic changes could be expected. These cells are most often found in greatest concentration at the caudal (pontine) levels not far above the nucleus of the motor root of the fifth cranial nerve.

Animal A of litter XXIII, in which the nerve had been bilaterally severed, and its control mate (animal E of litter XXIII) were killed forty-six days after operation. The brain and stem were removed from both animals. The stump of the fifth cranial nerve (the proximal branches from the sensory root) was easily identified as it entered the lateral portion of the pons. With this as a landmark, the brain stem of each animal was sectioned rosterally at the level of the midbrain and caudally well below the exit of the motor root of the fifth cranial nerve. This truncated segment of the stem was then fixed, sectioned, and stained appropriately for Nissl substance.

Serial sections of this segment of the stem were then examined for signs of reactionary chromatolysis in the cells of the mesencephalic nucleus. It is well to remember that anatomic structures are three dimensional and that the mesencephalic nucleus is no exception. For this reason, the cellular details in random cells of this constellation are by no means clear and defined, even in sections taken at any one level. Often the cytoplasm is visualized but the nucleus is ghost-like or drops out. This nucleus may or may not appear in the next section in series.

In our series the cells of the mesencephalic nucleus in control animal E of litter XXIII, killed forty-six days after operation, were as previously described (Fig. 9). They varied in number and size at different levels. The cells were smaller and fewer at the midbrain and larger and more numerous at the pontine levels. The cells of the nucleus at the caudal end (the area of greatest concentration) were large to medium-sized, pear-shaped, unipolar cells lying at the side of the fourth ventricle just above the nucleus of the motor root of the fifth cranial nerve. When seen, the nuclei were large, clear, and centrally placed. The nucleoli were round, dark, and centrally placed. The Nissl substance was quite well defined and evenly distributed through the whole cell. In number, size, and shape, these cells contrasted sharply with the large multipolar cells of the motor root of the fifth cranial nerve. Nor were they to be confused with cells of the loci caeruli lying close by (that is, just ventral to the lateral recess of the fourth ventricle). Cells of this nucleus were smaller and triangular, with two or three processes. They were rather uniformly pigmented.

In animal A of litter XXIII, killed forty-six days after bilateral nerve severance, certain cells of the nucleus showed several changes (Fig. 10). Animal A showed an acceleration in eruption rate of 13 per cent over the control, plus changes in pigment. The cells were swollen well beyond their mates. The nucleus, even when present in the affected cell, lacked definition and was eccentric in the cell. Not infrequently a clear halo rimmed what was left of the

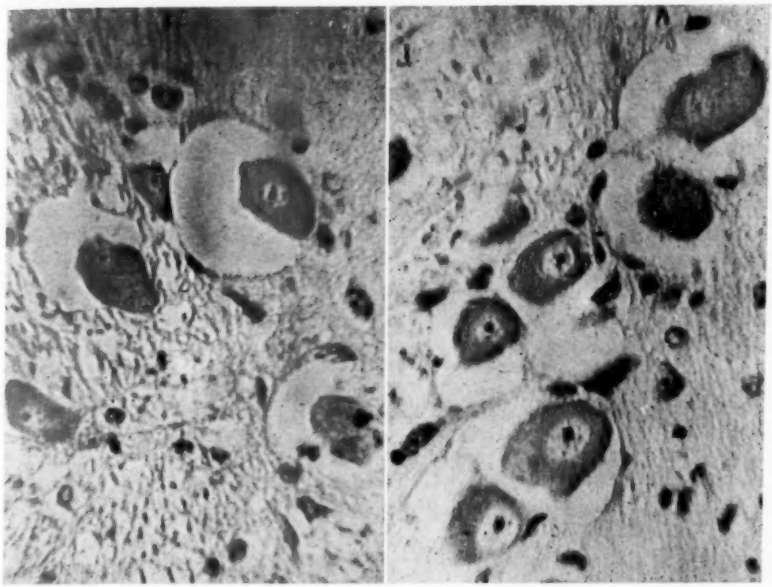

Fig. 11.—Mesencephalic nucleus at the same level in animal C of litter XXIII with unilaterally severed inferior alveolar nerve. (Nissl preparation.)

nucleus. There were some cells in which no nucleus could be found serially. Nissl substance, appearing at best as a faintly granular "cloud," seemed to have gone into partial solution in these cells.

In animal C of litter XXIII killed forty-six days after unilateral nerve severance, chromatolytic changes in the cells of the mesencephalic nucleus were limited to the nerve-severed side (Fig. 11). (There was a 27 per cent acceleration in eruption rate on the left side as compared to the right side; changes in pigment were also evident.) On the side not subjected to nerve severance the cell population was well within the "control" range. On the nerve-severed side individual cells of the group showed swelling of their cell bodies, eccentricity of their nuclei, and reduction of Nissl substance to a finely granular cloud.

DISCUSSION AND CONCLUSIONS

It should be clear at this time that the incisors and their investing structures (periodontium) do not stand alone. Thanks to a functional union of several related structures, the teeth are but part of a complex functional whole—a proprioceptive system. This system involves the upper and lower teeth, their supporting periodontal membranes, the muscles of mastication, the gingivae, the lips, and the hard palate. These are structures which provide an anatomic substrate for the reflex action of mastication. This reflex depends on the integrity of a neural arc (in fact, on all three of its phases—beginning, middle,

and end). The operation of nerve severance, unilateral or bilateral, deliberately interrupts at least one or both of the afferent arms of this arc and therefore may well result in a decrease in the functional efficiency of the reflex, however limited. It disturbs the integrity of the animal and thus affects the animal's equilibrium with its surroundings. This loss or deficit might well be greater because it occurs at a time of rapid growth and development of the animal. The nineteenth to the thirty-fifth days could well be called a truly critical period, when the animal not only changes from a liquid diet to solid food but also has to seek this new feed instead of being fed by its mother. Losses in functional efficiency thereafter would be cumulative.

Concerning the stimuli, the receptors, and the field of reception for this proprioceptive sensory system of fibers, Sherrington[3] has stated:

> The receptors which lie in the deep tissues appear adapted for excitation by changes going forward in the organism itself. The mechanical stress or compression which stimulates some deep receptor arises as the result of some antecedent reflex movement provoked through some surface receptor usually of the exteroceptive field.

Movements which ensue on the basis of external signals themselves cause muscle-stretch sensations. These serve to inform the animal of the correctness or incorrectness of this movement and of its relation to the external condition which gave rise to the given activity.

Concerning the reflex as a complex, coordinated whole, Sherrington[15] says:

> On the mouth's seizing a morsel the mandible, when it has closed, e.g., voluntarily on whatever is between the jaws pressing it against the gums and teeth and hard palate, by so doing, as is clear from observation of the reflex, produces a stimulus which tends reflexly to reopen the jaws. That done, the central rebound of the previously reflexly inhibited jaw closing muscles or rather their motoneurons, for the inhibition is central, sets in and tends to powerfully reclose the jaw again. The reclosure brings into operation once again the jaw opening stimulus. And so, after being started by a first bite, a rhythmic masticatory reflex tends to keep itself going so long as there is something between the teeth. . . . The centripetal impulse from the muscles and the teeth and supporting structures provide an important kind of spatial coordination which I have termed reciprocal innervation.

Here in life is a mechanism which serves to coordinate biting and chewing movements, a primitive mechanism phylogenetically evolved to meet the needs of the animal in its transition from dependence to free living. It is this mechanism of reflex action to which Taylor and Butcher[1] referred when they said:

> Awareness of the condition of the incisors must be furnished by sensory endings around the tooth, on the lips, tongue and palate. Response to this sensory information results in the control of special attritional and incisive activity both of which play a role in maintaining the optimum length of the teeth.

It is precisely the information provided by this proprioceptive system of fibers and the inhibition conferred by the reflex which controls the force of the bite and gives protection to the teeth of the control animals and results in damage up to and including fracture of the teeth in the animals that have undergone nerve severance. The inhibition conferred by this reflex is expressed in

terms of coordination in the biting and chewing activities of the control animals; its loss is expressed by imbalance in the control of both attritional and incisive activities in the nerve-severed animals.

This imbalance was further reflected in certain distortions of occlusion (that is, deviations of the lower teeth) among the experimental animals. This deviation was uniformly to the side of nerve severance in animals subjected to surgical intervention on one side. In the bilaterally denervated animals the direction of deviation, when it occurred, was unpredictable. That such deviation could not be attributed to surgical trauma to the pterygoid muscles or their nerve supply was proved by the absence of these changes following operations without nerve severance.

There is real unawareness in the denervated teeth. Functional stresses or pressures, even those of normal occlusion, are no longer transmitted. Stress is no longer stress unless it is transmitted. It is not transmitted in this instance because a part of the centripetal path is deliberately interrupted. Without transmission to the center, there is impairment in the integrating and coordinating activities of the center, with a resulting incoordinated response. In nerve-severed animals the subtle balance of reciprocal innervation which serves to control the abrasive and incisive activities, and hence the eruption rate of the teeth, is overset. There follows an acceleration in rate of eruption of one or both of the denervated teeth. For the same reason, an equivalent acceleration in the eruption rate occurs in a tooth or teeth deliberately relieved of functional stress or pressure (disked out of occlusion).

Losses of pigment were confined to the mandibular incisors. These changes were uniformly restricted to the nerve-severed tooth in the unilaterally denervated animals, and they occurred in both teeth in the bilaterally denervated animals. Such changes could hardly be interpreted as being either metabolic or vascular in origin. The striking difference between the thicknesses of enamel and dentine on the denervated tooth or teeth and on the normal control tooth is offered as evidence that the acceleration in rate of eruption of these teeth reduced the time for appositional growth and thus the time needed for deposition of pigment in the teeth.

SUMMARY

Following severance of the inferior alveolar nerve on one side, the incisor tooth on that side invariably exhibited an acceleration of eruption. When the inferior alveolar nerve was severed bilaterally, both teeth showed an acceleration of eruption far beyond the rate in the control animals of the same litter.

The teeth were notched in order that eruption rates could be measured and recorded. Notching was not attempted before the twenty-fifth to the thirtieth day in order to ensure degeneration of fibers in the distal segment and retrograde degenerative changes in the cells of origin of these fibers (that is, mesencephalic nucleus of the fifth cranial nerve). Degeneration of inferior alveolar nerve fibers at the periphery and chromatolytic changes in cells in the center were constant findings.

Careful studies by Corbin on the peripheral distribution of fibers rising in the mesencephalic nucleus and by Corbin and Harrison on the function of the mesencephalic nucleus and root of the fifth cranial nerve had previously demonstrated the actual links in a highly stable anatomic substratum for segmental activity. This neural arc served functionally to coordinate biting and chewing movements. Specialized receptors in this neural arc are situated in organs of movement and their appendages (muscles, teeth, and supporting structures). Tension in these receptors largely determines muscle sense and stretch information. Large and medium-sized myelinated fibers which have their origin in the mesencephalic nucleus and their end terminals in these receptors mediate proprioceptive impulses from the muscles of mastication and deep pressure from the teeth, periodontal membranes, gingivae, and soft palate. The operation of nerve severance deliberately interrupts the afferent limb of this arc. It is the sensory information from these receptors which is essential for the operation of a coordinated masticatory response. Lack of this information following on the heels of nerve severance leads to incoordination and imbalance in such vital activities as biting and chewing.

From this vantage point, it is clear that the incisors and their investing structures do not stand alone. Thanks to a functional union of several related structures, the teeth are but part of a complex functional whole—a proprioceptive system. It is precisely the deep pressure sensibility information provided by this system of fibers and the inhibition conferred by the reflex which control the force of the bite and protect the teeth of the control animals and result in damage to the teeth and supporting structures of the experimental animals. Responses based upon this proprioceptive sensory information result in control of the special attritional and incisive activities of the teeth, both of which play a role in maintaining the length of the teeth and hence in their rates of eruption.

It is with pleasure that the authors express their indebtedness to students, Mr. Jack Cushing and Mr. Harry Lumerman, for their care of the animals over long periods of time, for their help in notching teeth and recording eruption rates, and for their assistance in the preparation of charts. We are especially indebted to Mrs. Gloria Turner and Miss Elsie Dallas for their preparation of hundreds of sections, many of them stained with special silver techniques. We thank Mrs. L. Price for secretarial assistance.

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THE RESPONSE OF EXPERIMENTALLY INJURED ALVEOLAR BONE TO CULTURED CALF BONE IMPLANTATION IN DOGS

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INDUCTION of bone growth in areas of alveolar crest resorption associated with periodontal disease has long been the aim of many investigators. Experimentally created alveolar bone injuries and periodontal lesions in human beings have been exposed to different "bone-inducing agents" with varying degrees of success.[1-7]

The present study deals with the influence of cultured calf bone† on the healing and regeneration of experimentally injured alveolar crestal bone in young adult male dogs.

MATERIALS

The animals consisted of fourteen 1-year-old male dogs, each weighing approximately 15 pounds at the beginning of the experiment.

Twenty-eight surfaces were operated on in the fourteen dogs. In other words, each animal had both a control and an experimental side.

A specially prepared calibrated periapical roentgenographic film was used to record accurately any regeneration of alveolar crestal bone.

METHOD

After general anesthesia had been produced with Pentothal sodium, reverse flaps exposing the interproximal bone area between two contiguous teeth on the right and left sides of either mandible or maxilla were raised. The alveolar

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†Cultured calf bone prepared after the method of Tucker was provided through the courtesy of the Squibb Institute for Medical Research, New Brunswick, New Jersey.

bone was exposed to the crest, and care was taken not to disturb the covering soft tissues in order to prevent an opening from the injured area to the mouth through the operative site (Fig. 1). A periodontal probe was placed in a gingival cervical direction and, with an indelible pencil, a 3 mm. line was drawn vertically along the interdental alveolar crest. By means of a half-round burr under a stream of water, multiple holes were drilled, following the indelible line along the crest. A 701 fissure burr under water spray was used to connect these holes and to deepen this crater to 3 mm. in a buccolingual direction and 1 mm. mesiodistally.

The left mandible or maxilla was used as a control. Cultured calf bone was placed in the crater of the right side, filling it to its preoperative height. The flaps were returned to their original positions and sutured into place.

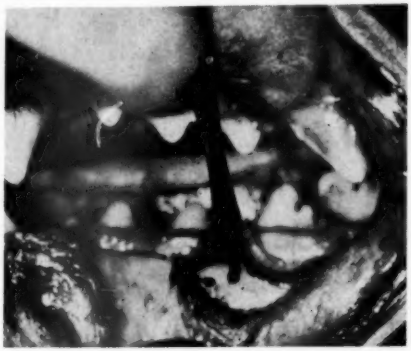

Fig. 1.—Photograph of the exposed alveolar bone between two contiguous teeth. Note raised reverse semilunar flap, with groove cut into the alveolar ridge.

At predetermined intervals, the operative sites were observed by clinical probing of the depth of the gingival crevice. Clinical photographs and intraoral roentgenograms were taken at this time. The intraoral roentgenograms were calibrated in the following manner in order that crestal bone changes might be observed more accurately:

The lead foil was removed from an ordinary periapical roentgenogram. With a pointed instrument and a millimeter rule, square boxes measuring 10 by 10 mm. were drawn to cover the entire surface of the foil (Fig. 2). Horizontal lines, 2 mm. apart, were drawn in a vertical direction on the line dividing the foil in half. Care was taken not to puncture the foil with the sharp drawing instrument. The foil marking device was placed over an unexposed periapical roentgenogram (of the extra fast variety) 8 inches from the tip of the cone on the dental x-ray unit, and the film was exposed for one second of its two-second exposure time. The roentgenograms were placed in the operative sites of the animals with the aid of an ortholator using a fixed angle of sixty degrees. The films were then exposed for an additional second.

The animals were killed at specified intervals during a nine-month period: two animals immediately after operation, two at three weeks, one at six weeks,

four at three months, and five at nine months. The jaws were dissected out and fixed in formalin. The specimens were then decalcified in 5 per cent nitric acid, embedded in colloidin, and prepared for histologic study. Serial sections were obtained from each operative specimen.

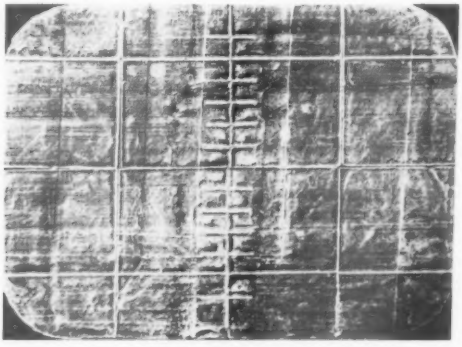

Fig. 2.—Photograph of the calibrated lead foil used to mark unexposed periapical film.

GROSS OBSERVATION

The animals progressed extremely well postoperatively. No apparent examples of intolerance to the cultured calf bone were observed. The dogs gained an average of 5 pounds and remained healthy during the entire observation period.

ROENTGENOGRAPHIC AND HISTOLOGIC OBSERVATIONS

Operative Site Immediately After Operation.—On radiographic examination, the control operative site showed a radiolucent area in the interproximal septum (Fig. 3). Histologically, the control crater appeared as an empty space surrounded by necrotic periodontal fibers. The bone immediately surrounding the site of injury also showed necrotic changes as evidenced by empty lacunae in the area. The epithelial attachment level appeared not to be disturbed and was located at the cementoenamel junction (Fig. 4).

The operative site filled with cultured calf bone appeared slightly more radiopaque in the intraoral roentgenograms than the control site (Fig. 5). Histologic examination of the area filled with cultured calf bone showed many small bone and cartilage spicules surrounded by necrotic debris within the experimentally formed crater (Fig. 6).

Operative Site Three Weeks After Operation.—The operative control site showed a slight radiolucency in the crestal portion of the interproximal alveolar septum (Fig. 7). Histologically, this area showed marked endosteal resorption extending into the alveolar bone proper near the crest. The central portion of the interproximal septum was filled with young connective tissue elements. Some areas of new bone formation were also present (Fig. 8).

Fig. 3.

Fig. 5.

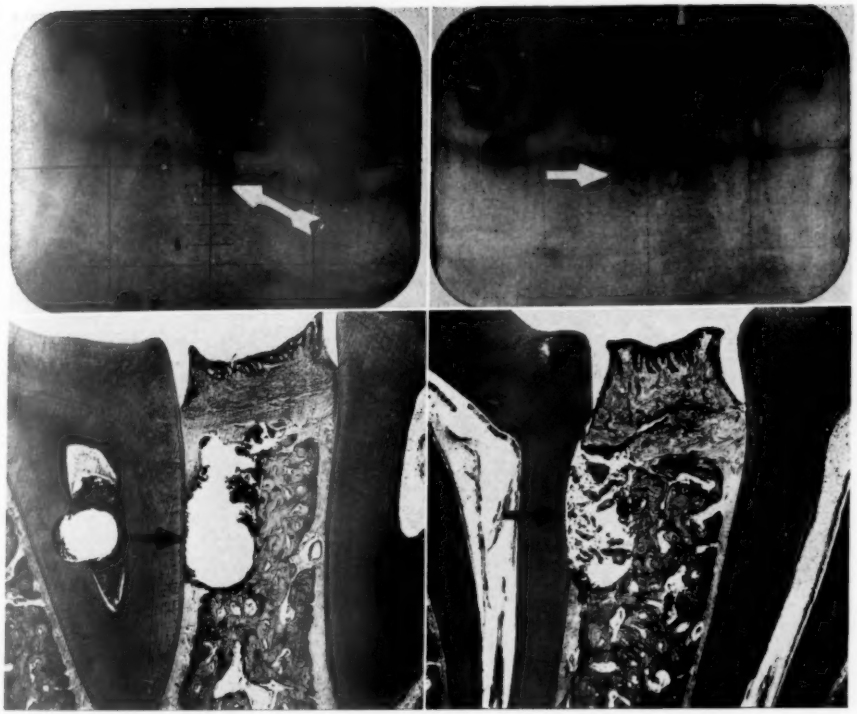

Fig. 4.

Fig. 6.

Fig. 3.—Roentgenogram of the operative control site immediately after operation. Note the radiolucent area at the interdenal septum (arrow).

Fig. 4.—Photomicrograph of the operative site shown in Fig. 3. Note the area of injury in the interdental septum (arrow). (Hematoxylin and eosin stain. Magnification, × 10; reduced ¼.)

Fig. 5.—Roentgenogram of the operative site filled with cultured calf bone, immediately after operation. Note the slightly more radiopaque appearance of the site of injury (arrow).

Fig. 6.—Photomicrograph of the operative site shown in Fig. 5. Note the presence of bone chips in the experimentally formed crater (arrow). (Hematoxylin and eosin stain. Magnification, × 10; reduced ¼.)

The operative site filled with cultured calf bone appeared more radiopaque on roentgenographic examination (Fig. 9). Histologic study of the site showed the area to be filled with small bone spicules whose surfaces were surrounded by osteoblasts in most instances. New bone formation was also present throughout the crater (Fig. 10).

Operative Site Three Months After Operation.—The control site showed a slight crestal radiolucency (Fig. 11). Histologically, gingival recession with ulceration was noted. A marked cellular infiltration was present subepithelially. The alveolar crest showed some osteogenic activity (Fig. 12). This healing response could not be predicted from the roentgenographic appearance of the operative site.

Fig. 7.

Fig. 9.

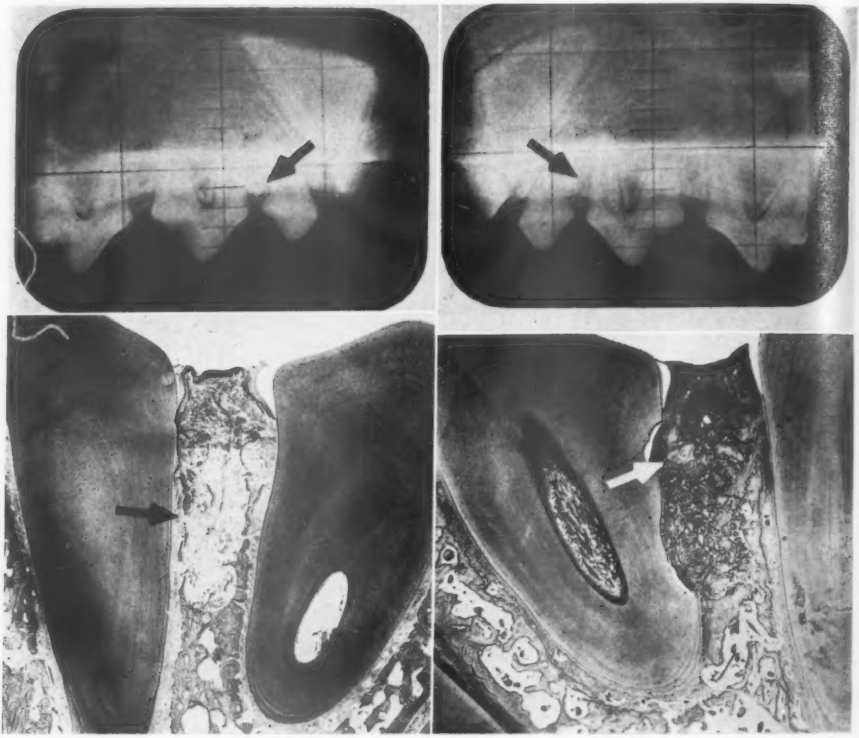

Fig. 8.

Fig. 10.

Fig. 7.—Roentgenograpam of the operative site three weeks after operation. Note the radiolucency in the interdental alveolar crest (arrow).

Fig. 8.—Photomicrograph of the operative site shown in Fig. 7. Note the endosteal bone resorption in the interdental alveolar crest (arrow). (Hematoxylin and eosin stain. Magnification, × 10; reduced ¼.)

Fig. 9.—Roentgenogram of the operative site filled with cultured calf bone, three weeks after operation. Note the more radiopaque appearance of the operative site as compared with that seen in Fig. 7 (arrow).

Fig. 10.—Photomicrograph of the operative site shown in Fig. 9. Note the cellular activity around the bone chips (arrow). (Hematoxylin and eosin stain. Magnification, × 10; reduced ¼.)

The site treated with cultured calf bone showed a marked crestal radiolucency (Fig. 13). Histologically, the epithelial attachment was located at the cementoenamel junction. An inflammatory infiltrate was present subepithelially. The crestal alveolar bone proper appeared intact; however, a very striking enlargement of the marrow spaces of the interproximal septum was noted which may have been the result of experimental injury (Fig. 14).

Operative Site Six Months After Operation.—Slight gingival recession and crestal resorption were present at the control site. The experimental site showed varying degrees of gingival recession and crestal resorption in different animals.

Fig. 11.

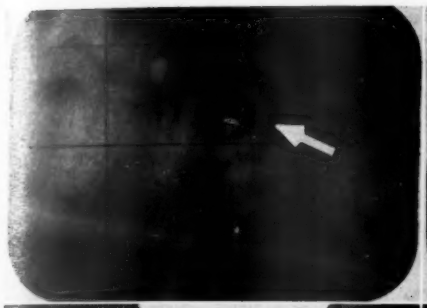

Fig. 13.

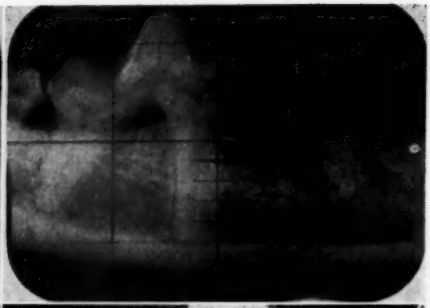

Fig. 12.

Fig. 14.

Fig. 11.—Roentgenogram of the operative control site three months after operation. Note the slight crestal radiolucency.

Fig. 12.—Photomicrograph of the operative site shown in Fig. 11. Note osteogenic activity at the crest (arrows). (Hematoxylin and eosin stain. Magnification, × 10; reduced ¼.)

Fig. 13.—Roentgenogram of the operative site filled with cultured calf bone, three months after operation. Note the marked crestal radiolucency (arrow).

Fig. 14.—Photomicrograph of operative site shown in Fig. 13. Note the intact alveolar crest with marked enlargement of the marrow spaces within the septum (arrow). (Hematoxylin and eosin stain. Magnification, × 10; reduced ¼.)

Operative Site Nine Months After Operation.—Both the control and the experimentally treated sites showed gingival recession with varying degrees of crestal bone repair. No distinct difference could be noted between the healing response of injured crestal bone and that seen following injury and cultured calf bone implantation.

These observations were evident both roentgenographically and histologically (Figs. 15 to 18).

COMMENT

Of necessity, roentgenographic studies of changes in alveolar bone require accurate roentgenograms. Patterson[8] introduced a calibrated film which was

Fig. 15. Fig. 17.

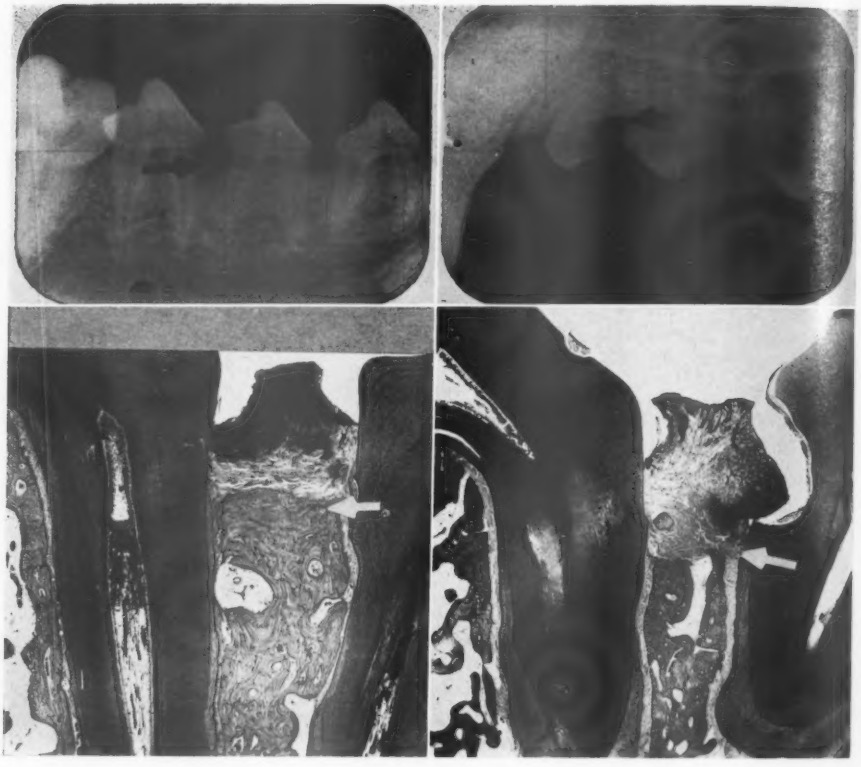

Fig. 16. Fig. 18.

Fig. 15.—Roentgenogram of the operative control site nine months after operation. Note evidence of slight crestal resorption.

Fig. 16.—Photomicrograph of the operative site shown in Fig. 15. Note the apparently healed interdental septum. (Hematoxylin and eosin stain. Magnification, × 10; reduced ¼.)

Fig. 17.—Roentgenogram of the operative site filled with cultured calf bone, nine months after operation. Note the alveolar crest resorption.

Fig. 18.—Photomicrograph of the operative site shown in Fig. 17. Note the crestal resorption to a level apical to the experimentally created notch in the root.

manufactured in limited numbers by the DuPont Company. The present study outlines a quick and efficient method for calibrating dental roentgenograms which is easily reproducible. It is of interest, however, that, even under these optimal investigative conditions, the roentgenogram did not always mirror histologic findings accurately. The intraoral roentgenogram shown in Fig. 11 shows a radiolucent area at the interproximal alveolar crest which might be interpreted as resorption of the alveolar crest. The histologic specimen (Fig. 12), however, shows areas of crestal apposition. Figs. 13 and 14 show further variations between the roentgenographic and histologic appearances of the alveolar crest. These observations again call attention to the difficulties inherent in roentgeno-

graphic interpretation of minute alterations in crestal bone level, especially with regard to the slight changes in crest resorption and bone repair associated with gingival inflammation and healing.

SUMMARY AND CONCLUSION

Experimentally produced craters in the alveolar crestal bone of twenty-eight interproximal surfaces in fourteen 1-year-old male dogs were created. In each animal cultured calf bone was used to fill the crater on the experimental side, while the control side was left untreated. Periapical roentgenograms with specially prepared calibrations were taken at the site of injury. The animals were killed at specified intervals during a nine-month period. The jaws were then dissected out and prepared for histologic study.

The following observations were made:

1. The cultured calf bone was well tolerated in all animals.
2. More pronounced osteogenic action was seen in the crater filled with cultured calf bone in the three-week specimens than was observed in the control crater.
3. Examination of the operative sites six to nine months following operation showed gingival recession with crestal resorption and evidence of some bone repair. No difference could be observed between the control and experimental specimens.
4. Roentgenographic interpretation of alveolar crestal activity did not always coincide with the histologic appearance of the specimen.

The authors wish to thank Helen Rosenman, B.A., for her technical assistance in the preparation of this study.

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Section of the

FEDERAL DENTAL SERVICES

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PREGNANCY TUMOR

Report of a Case

*Jack Traiger, Captain, DC, USA**

Oral Surgery Section, Post Dental Service, Fort Jay, Governor's Island, N. Y.

THERE is a question in the minds of some pathologists as to whether or not the tumors associated with puberty, menses, pregnancy, and menopause should be considered separate entities. These tumors are single or multiple outgrowths from the gingiva that occur during the various sexual changes of life and are most prominent at the peak of hormonal imbalance. They are classified according to the condition which appears to be responsible for their existence. Some investigators, however, do not recognize these outgrowths as individual lesions and prefer to think of them as types of gingivitis or granuloma pyogenicum.[1]

ETIOLOGY

Imbalance of hormonal production results in the appearance of these lesions. Local irritations, particularly unclean mouths and broken-down teeth, play a secondary role.

SIGNS AND SYMPTOMS

Onset occurs generally in the third month of pregnancy. Gingivitis and hypertrophy of the gingival margin, especially the interdental papilla, are always present (Fig. 1). The tumorlike formations usually occur on both sides of the dental arch simultaneously, often producing separation of the teeth. They may occur singly or as multiple lesions. They develop into spherical red bodies, often with a bluish hue, which bleach out on pressure (Fig. 2). They are prone to food impaction and ulceration. When large, they may be injured

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during mastication; such injury is followed by long-continued hemorrhage. Generally these tumors are no larger than beans, but occasionally they grow to a very large size. It should also be remembered that tumors in general may be stimulated to accelerated growth during pregnancy. On termination of pregnancy they tend to recede in some (but not all) instances.[2]

Fig. 1.—Labial segment of pregnancy tumor extending between mandibular incisors.

Fig. 2.—Pregnancy tumor. Large lingual mass in woman eight months pregnant.

HISTOPATHOLOGY

The fibrous connective tissue stroma is almost completely replaced by a marked proliferation of endothelial cells. This is in the form of many small, patent blood vessels. The cells that line the endothelial spaces are plump and not excessive in number. There may be a chronic or an acute inflammatory

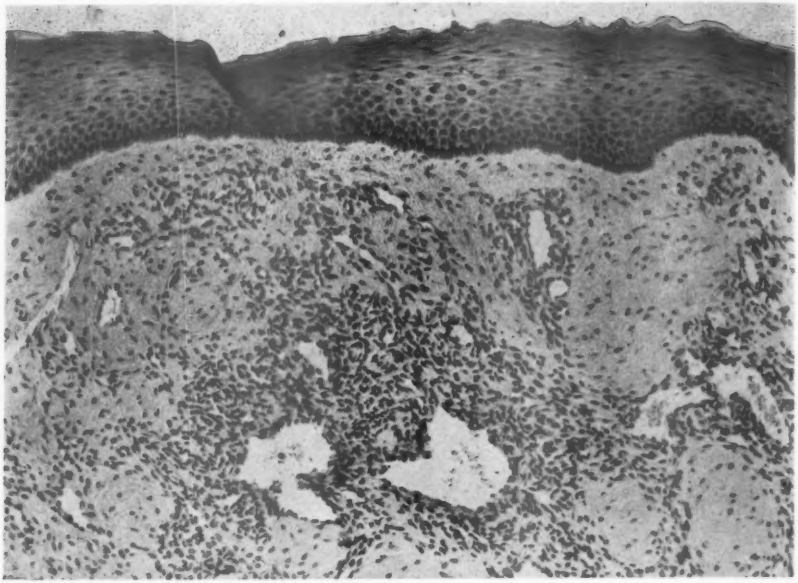

Fig. 3.—Photomicrograph of pregnancy tumor. This is a fibrohemangioma type of lesion with hydropic changes in the epithelium.

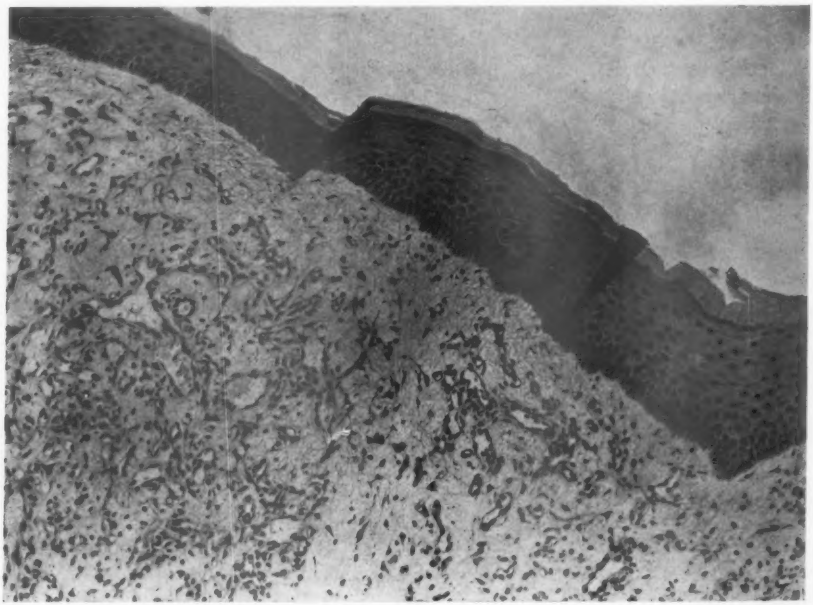

Fig. 4.—Photomicrograph of pregnancy tumor. The covering squamous epithelium is normal in thickness.

exudate; the latter is seen particularly when there is ulceration. The covering epithelium is of the squamous variety and may be thinned or relatively normal in thickness (Figs. 3 and 4).

These proliferations may mimic other more serious conditions; therefore, tissue investigation is mandatory if the tumor continues to grow.

CASE REPORT

R. H., a 23-year-old housewife, was seen in the eighth month of pregnancy, complaining of a large mass in her mouth which she had first noticed five months previously. She stated that it was becoming progressively larger, that it interfered with eating, and that it bled easily.

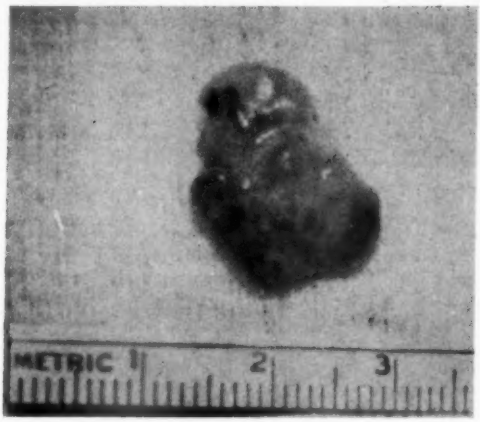

Fig. 5.—Surgical specimen of pregnancy tumor.

Fig. 6.—Surgical site protected by packing of both surfaces.

The mass was located on the lingual surface of the right mandibular incisors, covering the crowns of the teeth on the lingual aspect and extending downward into the floor of the mouth. It was pink with a bluish hue, soft, and quite movable. It was elevated easily and appeared to be attached by a thin stalk to the lingual mucosa. On the labial surface there

was an enlarged interdental papilla which appeared to be directly connected to the larger lingual mass but which caused no separation of the teeth. There was some blanching upon pressure but no associated pain. Examination showed a well-cared-for mouth. The mass was removed under local anesthesia. With an electrocautery, the tumor masses which ex-

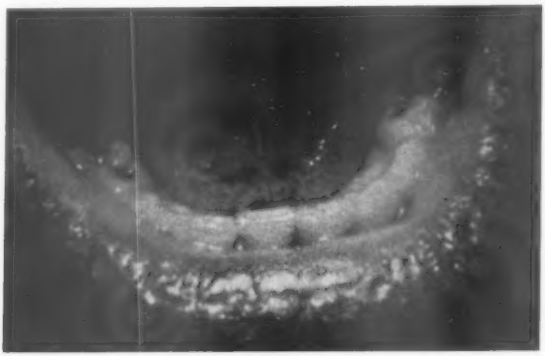

Fig. 7.—Uneventful healing with no recurrence.

tended from the gingival margin on both the labial and the lingual aspects of the mandible were excised by cutting through the pedicle (Fig. 5). The ensuing hemorrhage was arrested by electrocoagulation. A surgical pack mixed into a semisolid paste was applied to the teeth on the inner and outer surfaces to protect the raw surfaces that resulted from the surgical procedure (Fig. 6). Healing was uneventful, and there was no recurrence[3] (Fig. 7).

Tissue analysis confirmed the preoperative diagnosis of pregnancy tumor.

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FLUORESCENCE MICROSCOPY IN EXFOLIATIVE CYTOLOGY OF ORAL CARCINOMAS

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FLUORESCENCE microscopy (FM), utilizing fluorochrome acridine orange (AO), has proved valuable in the detection of carcinoma cells in smears of body secretions.[1-3] Some investigators have found it more sensitive than the standard Papanicolaou technique.[1, 2] In a preliminary report, my associates and I[3] commented on the advantages and disadvantages of FM in general exfoliative cytology, including oral cytology. The purpose of the present report is to relate additional experiences with this modality in the diagnosis of carcinoma of the mouth and related lesions.

MATERIALS AND METHOD

Direct oral smears were taken from patients with clinically obvious carcinoma, leukoplakia, or ulcer. The smears from the carcinoma group were obtained prior to, during, and following radiotherapy—or prior to operative removal.

The smears were fixed in equal parts ether-alcohol (70 per cent) for at least five minutes prior to staining with AO. The staining technique of Bertalanffy,[1] and of Dart and Turner[2] were used during the initial phase of this study, but the latter was abandoned because of the lack of intense cytoplasmic fluorescence.

Our modification of the Bertalanffy technique has been described elsewhere.[3] The smears were examined with the fluorescence microscope using blue-violet radiation at wave lengths of 500 to 800 millimicrons. The screening was done at a magnification of × 150, and morphologic study at × 600. The mean examination time per smear was one minute.

After the smears had been examined by AO-FM, the coverslips were removed, the smears destained in 50 per cent ethyl alcohol for several minutes, restained by the routine Papanicolaou technique, and re-examined. The mean examination time for a Papanicolaou-stained smear was three minutes.

The smears were reported as positive, suspicious, or negative.

TABLE I

CELL TYPE	CYTOPLASM	NUCLEUS
Polymorphonuclear leukocytes	Colorless or pale green	Dull to bright green, depending upon extent of degenerative change Degenerating "pus" cells large and smudged
Plasma cells (uncommon)	Bright orange	Moderate green
Erythrocytes	No fluorescence; invisible	
Bacteria	Brilliant orange	
Macrophages (uncommon)	Dull brown to bright orange; frequent nonfluorescent vacuoles, often with brightly fluorescent, ingested bacteria	Green to yellow; variation in intensity of fluorescence; characteristic bean shape
Benign superficial squamous cells	Pale green, almost invisible	Green, slightly brighter than cytoplasm, often pyknotic; nucleoli rare, bright orange when present
Benign parabasal cells (uncommon)	Bright green to pale orange	Bright green to moderate yellow; fluorescent particles widely dispersed indicating scanty chromatin; nucleoli single, small, bright orange
Hyperplastic squamous cells	Moderate orange; quantity intermediate between parabasal and superficial squamous cells	Bright green to moderate yellow; prominent single brilliant orange nucleolus
Well-differentiated malignant squamous cells	Dull or bright green to pale orange, abundant	Moderate or bright green to pale yellow; irregular clumps of fluorescent particles; rare nucleoli; naked nuclei common
Less mature malignant squamous cells	Bright green to brilliant orange, frequently vacuolated	Bright yellow; large, single or multiple brilliant orange nucleoli; naked nuclei common
Irradiated malignant squamous cells	Almost invisible green to bright orange; large cells, often coated with bacteria, vacuoles common	Pale green to brilliant yellow; large; often devoid of cytoplasm; occasionally vacuolated; brilliant orange large nucleolus or nucleoli

RESULTS

The cell types and their appearance by AO-FM are shown in Table I.

Smears From Clinically Obvious Carcinomas Prior to Treatment.—Although the smears were taken directly from the surface of the neoplasms, the predominating epithelial cell in most instances was the benign superficial squamous cell. Since these cells exhibited little or no fluorescence, the smears could be scanned rapidly, and atypical cells stood out brilliantly against the black background. Frequently benign squamous cells were coated with brilliant orange bacteria, but this fluorescence was differentiated readily from that of the cytoplasm of malignant cells by the spotty distribution, and the identification of bacteria at higher magnifications. In smears which were overstained

or stained with buffer which was too alkaline, the nuclei of leukocytes fluoresced bright yellow, and under scanning magnifications clusters of these cells were troublesome. This difficulty was corrected by returning the smears to the buffer solution for additional destaining.

Erythrocytes, even when abundant, did not obscure the epithelial cells, since the former were nonfluorescent and therefore invisible.

Malignant cells varied markedly in number present and intensity of fluorescence. In some smears only a few such cells were present, either singly or in clusters, whereas in others they made up over 90 per cent of the epithelial cell population. On the average, about 15 per cent of the epithelial cells exhibited *morphologic* features of malignancy.

Poorly differentiated carcinoma cells were brilliant, with intense orange cytoplasm and nucleoli, and bright yellow nuclei. The intensity of fluorescence was decreased by maturation or degenerative change. There appeared to be an inverse ratio between the degree of cornification and the intensity of cytoplasmic fluorescence. Flakes of keratin, common in the Papanicolaou preparations, rarely were discernible by AO-FM.

The inhibition of fluorescence by degenerative change was less constant, and some degenerating cells were represented by naked pale green nuclei. Others were visible only as faint shadows, despite their easy recognition in the Papanicolaou controls. On the other hand, bright fluorescence of many carcinoma cells was preserved even though the same cells appeared smudged, poorly stained, or distorted in the Papanicolaou smears.

Smears From Irradiated Carcinomas.—No appreciable changes were noted during the first few days of x-ray or cobalt^{60} irradiation. By the end of the first week of treatment, certain morphologic alterations in benign and malignant cells became evident. These were cellular, nuclear, and nucleolar enlargement, more binucleated benign cells and multinucleated malignant cells, and cytoplasmic vacuoles. There was often a sudden increase in the number of exfoliated malignant cells during the early phase of treatment. These alterations were observed in the AO and Papanicolaou smears.

There was a gradual reduction in fluorescence during irradiation, and a conversion from yellow nuclei and orange cytoplasm to green nuclei and cytoplasm; however, these changes were variable, and in many instances the luminescence remained constant until the carcinoma cells disappeared, usually in the late phases of treatment.

There was one striking difference between the appearance induced by irradiation and that caused by degenerative change or maturation. In the latter, there was relatively more rapid reduction in the fluorescence of cytoplasm than of nuclei, while irradiated cells showed proportionately greater decrease in nuclear brightness, resulting in bright orange cytoplasm and pale green nuclei. Nucleoli became more prominent during treatment because of an increase in size with preservation of the intensity of fluorescence.

The postirradiation cases were of three types: (1) those in which there was clinically apparent residual or recurrent neoplasm, (2) those in which the tumor site was indurated or ulcerated, and (3) those in which there was a

normal-appearing mucosa. In each category there was good correlation between the cytologic findings of AO-FM and those of the Papanicolaou-stained smears. Malignant cells were identified in smears from patients who had clinically obvious residual or recurrent neoplasm, and in some of those in whom the clinical evidence was less definite. These smears differed from the pretreatment smears in the relative sparcity of carcinoma cells, often requiring prolonged search. In the absence of residual mucosal abnormalities, the smears disclosed only enlarged, normal, superficial squamous cells with few or no inflammatory cells. In a few cases, particularly those of radionecrosis and ulcer it was difficult to differentiate atypical regenerating squamous cells from malignant cells in both the AO and the Papanicolaou preparations. The cytoplasm of these cells exhibited moderately bright orange cytoplasm and bright green or moderately bright yellow nuclei on AO-FM. Large, brilliant nucleoli occasionally were present. The intensity of fluorescence of these hyperplastic cells did not approach that of *viable* neoplastic cells but exceeded that of many mature or degenerating squamous carcinoma cells. The hyperchromasia and enlargement of the nuclei of these hyperplastic cells also presented interpretive difficulties in the Papanicolaou smears.

Smears From Leukoplakia and Ulcers.—Smears from mucosal white patches, which histologically lacked cellular atypism, consisted of superficial squamous cells with pyknotic or absent nuclei. These cells exhibited so little fluorescence that it was difficult to find the smeared material on the slide. When restained by the Papanicolaou technique the cytoplasm of these cells was bright red, orange, or yellow, and the morphologic appearances were similar to those seen in the AO preparations. In cases of "true" leukoplakia, that is, mucosal thickening and atypism, hyperplastic cells were demonstrated by both AO and the standard stains. Similar cells were obtained from the benign ulcers, but the evidence of cornification seen in leukoplakia was lacking.

In cases of early carcinoma arising in leukoplakia or in clinically innocent ulcers, suspicious cells were found which met the criteria already described for the mature type of malignant squamous cells.

In 525 of 669 oral smears (78.5 per cent) identical results were obtained by the two methods. If the positive and suspicious groups are considered as one, the agreement was 86.9 per cent. Among the 332 specimens which were positive by one or the other modality, 265 (79.8 per cent) were positive by AO-FM, and 293 (88.3 per cent) by the Papanicolaou technique.

The sensitivity of the combined methods was 11.7 per cent (suspicious reports excluded) greater than that of the Papanicolaou method alone, and 20.2 per cent greater than that of AO-FM alone.

A review of the specimens which were positive only in the Papanicolaou controls revealed, in each instance, that the malignant cells were very sparse and were of the poorly fluorescing variety.

DISCUSSION

Previous investigations have demonstrated that the protein metabolism and the nucleic acid content of actively proliferating cells are increased. This is

especially true of most carcinoma cells.[4] The application of AO-FM to exfoliative cytology is based upon the affinity of the metachromatic fluorochrome, acridine orange, for nucleic acids—the ribonucleic acid of cytoplasm and nucleoli fluorescing bright green to orange, and the desoxyribose nucleic acid of nuclei fluorescing bright green to yellow. The great majority of malignant squamous cells in direct oral smears, because of high nucleic acid content, exhibited sufficient fluorescence to permit rapid detection and unequivocal differentiation from normal squamous cells. The latter were barely visible in the AO-FM preparations.

Some well-differentiated or degenerating malignant squamous cells, especially when cornified, showed minimal fluorescence, probably indicating less rapid metabolic activity. In fact, some of these cells were not as bright as benign hyperplastic or regenerating squamous cells found in healing ulcers or areas of radionecrosis. This is not surprising since such cells may have greater mitotic activity and faster growth than the less viable cells of a neoplasm. In most smears there were sufficient brightly fluorescing carcinoma cells to permit positive diagnosis, but some false-negatives resulted from the absence of bright cells. On the other hand, the poorly fluorescing type of squamous carcinoma cell was readily detected in the Papanicolaou-stained smears because the acidophilic cytoplasm stained intensely with the orange-G stain in this procedure.

Some carcinoma cells which stained poorly or exhibited swelling, distortion, or fragmentation in the Papanicolaou preparations retained brilliant fluorescence. In retrospect, it was noted that most of these cells were in smears which exhibited changes indicative of prefixation drying. It is well known that the Papanicolaou staining procedure does not permit drying of the smear prior to fixation. Fluorescence may be more sensitive to degenerative change than to in situ or in vitro autolysis, whereas in the Papanicolaou smears the reverse appears to be true.

Although cytoplasmic fluorescence was, in general, inversely proportional to the degree of keratinization, there was no difference in the *shade* of color of cornified and noncornified superficial squamous cells. The lack of fluorescence of keratin is unfortunate, since the flakes of keratin demonstrated so well in Papanicolaou smears may be the first clue to the cytologic diagnosis of carcinoma. For this same reason, we favor the standard Papanicolaou technique for the cytologic study of leukoplakia and mucosal ulcers.

In the course of natural maturation and aging, cytoplasmic fluorescence was lost more rapidly than was nuclear fluorescence. In contrast, therapeutic irradiation affected nuclear fluorescence more rapidly, resulting in malignant cells with bright orange cytoplasm and nucleoli but with very pale green nuclei. These cells correspond to the "B" cells described by Caspersson and Santesson[4] who noted decreased nucleic acids and large prominent nucleoli in cells from less viable portions of carcinoma. Conversion of this AO-FM cytologic profile from preponderance of cells with brilliant yellow nuclei to type "B" cells with pale green nuclei frequently preceded rapid disappearance of malignant cells during the sequential cytologic studies of irradiation effect.

SUMMARY AND CONCLUSIONS

In a comparative study of 669 direct smears from oral carcinomas, leukoplakia, or ulcers by acridine orange–fluorescence microscopy (AO-FM) and by the standard Papanicolaou method, there was agreement in 86.9 per cent of the specimens. The mean examination time per smear was one minute for the AO smears and three minutes for the Papanicolaou smears.

Poorly fluorescing cells, resulting from degenerative change or maturation, accounted for most of the false-negative results. However, AO-FM seems to be less affected by autolysis, especially the drying of smears prior to fixation, than is the Papanicolaou stain.

In the "natural" process of maturation or degenerative change of malignant squamous cells, cytoplasmic fluorescence decreased more rapidly than does nuclear fluorescence. Therapeutic irradiation reverses this sequence, resulting in carcinoma cells with pale green nuclei but bright orange cytoplasm and nucleoli. These may represent "sterilized" carcinoma cells.

The author wishes to acknowledge the helpful suggestions of Dr. Ludwig von Bertalanffy and Dr. Felix Bertalanffy, and the technical assistance of Mrs. Pearl Hill and Mr. Darrell McCaslin.

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ANNOUNCEMENTS

American Association of Endodontists

The annual meeting of the American Association of Endodontists will be held at the Fontainebleau Hotel in Miami Beach, Florida, Feb. 11 to 14, 1962. The theme of the meeting will be "The Biology of the Apical and Periapical Tissues." Drs. S. N. Bhaskar, Harry Blechman, D. Walter Cohen, Paul Sicher, and C. E. Wilde, Jr., will participate as clinicians.

American Academy of Maxillofacial Prosthetics

The annual session of the American Academy of Maxillofacial Prosthetics will be held at the Benjamin Franklin Hotel in Philadelphia, Pennsylvania, Oct. 11 to 14, 1961.

The program promises to be one of the most exciting and informative sessions ever held by this Society. The two and one-half day meeting is divided into sections: (1) Acquired Defects; (2) Congenital Defects; (3) Implants; and (4) Surgery and Surgical Prosthesis.

American Society of Oral Surgeons

The first International Conference on Oral Surgery, sponsored in conjunction with the Royal College of Surgeons of England, will be held at the Royal College in London, July 1 to 4, 1962. A bulletin is available on request. The program will include symposia on the temporomandibular joint and on maxillofacial injuries, in addition to a wide variety of scientific papers and discussion. Papers will be presented by essayists from North, South, and Central America, the United Kingdom, Europe, Africa, and Asia. Visitors attending the Conference will also have an opportunity to observe surgical procedures in the hospitals of London as a part of the Conference program.

Extensive social and ladies programs have been arranged by the Joint British-United States Committee. Features of the social program will be a banquet at London's famed and historic Guildhall and a reception by H. M. Government.

For additional details and bulletin, dentists and physicians in the United Kingdom and Europe should write Dr. Terence Ward, c/o Royal College of Surgeons, Lincoln's Inn Fields, London, W. C. 2, England. Dentists and physicians in the United States and other countries should write Mr. D. C. Trexler, American Society of Oral Surgeons, 840 N. Lake Shore Dr., Chicago, Illinois.

American College of Dentists

The New England Section of the American College of Dentists will hold its fall meeting on Wednesday, Nov. 1, 1961, at the Statler-Hilton Hotel in Boston, Massachusetts. Dr. Otto Brandhorst, secretary of the College, will be the guest speaker.

Dental Association Holds Hospital Seminar

The second Advanced Institute on Hospital Dental Service will be held Nov. 28 to 30, 1961, in Chicago, Illinois. It will be sponsored by the American Dental Association in cooperation with the American Hospital Association and will convene in the latter's headquarters in Chicago.

Program planning is being headed by Dr. Gerard J. Casey, Secretary, Council on Hospital Dental Services, American Dental Association.

American Dental Society of Anesthesiology

The Society will hold its eighth annual meeting at the Statler-Hilton Hotel in New York City, Oct. 13 to 15, 1961. For program and further details, write to Dr. J. D. Whisenand, 319 Bloomington St., Iowa City, Iowa.

Rowe Smith Memorial Foundation

The eighth annual seminar will be held Nov. 30 to Dec. 3, 1961, at the Fly-n-Fish Lodge in Karnack, Texas.

The subject will be "Disturbed Carbohydrate Metabolism." Topics to be covered include epidemiology and biochemistry of disturbed carbohydrate metabolism at the cellular level; dietary and hormonal influences on blood sugar level; methods of detection of disturbances of carbohydrate metabolism; clinical types of diabetes mellitus; anthropometry and carbohydrate metabolism; hypoglycemia; influence of emotional factors on glucose metabolism; and the treatment of diabetes mellitus.

The moderator will be D. Walter Cohen, Director of Periodontia, University of Pennsylvania School of Dentistry. Essayists include Donald W. Seldin, Professor and Chairman, Department of Internal Medicine, University of Texas Southwestern Medical School, and E. Cheraskin, Chairman of the Department of Oral Medicine, University of Alabama Dental School.

Those interested can obtain further information by writing the Rowe Smith Memorial Foundation, 501 State National Bank Bldg., Texarkana, Arkansas.

Symposium on Recent Developments in Research Methods and Instrumentation

Final plans have been announced for the eleventh Annual Instrument Symposium and Research Equipment Exhibit to be held October 9 to 12 and October 10 to 13, respectively, at the National Institutes of Health in Bethesda, Maryland. The NIH is the principal research center of the United States Public Health Service.

All persons having a professional or technical interest in research instrumentation are invited to attend the symposium and view the exhibit.

For additional information, write or call James B. Davis, National Institutes of Health, Public Health Service, Bethesda 14, Maryland (Phone: Oliver 6-4000, extension 2315).

Tufts University

The Department of Periodontology announces the establishment of a Registry of Gingival Disease. Practitioners are invited to submit gingival biopsies for diagnosis. Additional pertinent information will be provided by the Registry. Necessary forms and mailing containers will be sent on request. There is no charge for this service.

Interested persons may write to Tufts University School of Dental Medicine, 136 Harrison Ave., Boston 11, Massachusetts.

Mount Sinai Hospital

The Department of Dental and Oral Surgery announces that its proposed combined two-year residency in association with the School of Dental and Oral Surgery of Columbia University has been cancelled. The Mount Sinai Oral Surgery Service nevertheless will conduct a two-year oral surgical residency program.

Veterans Administration Medical Teaching Group Hospital

One rotating dental internship and two residencies in prosthodontia will be available for the year beginning July 1, 1962.

Information and application forms may be obtained from the Chief Dental Service, Veterans Administration Medical Teaching Group Hospital, Memphis, Tennessee.

Mount Sinai Hospital

The Department of Dental and Oral Surgery announces that the first of its 1961-1962 Wednesday night scientific meetings will be held at 8 P.M. on Oct. 25, 1961, in the surgical amphitheater on the fifth floor of the main building, Mount Sinai Hospital, 100th St. and Fifth Ave., New York, New York.

The subject of the meeting will be "Diagnosis and Management of Cleft Palate Problems." Members of the dental and allied professions are welcome.

First District Dental Society

The Postgraduate Education Department presents the following courses:

The Use of Precision Attachments in Partial Denture Construction. Nov. 3, 1961. Philip Edelman.

Principles of Operative Procedures. Nov. 3, 1961. Wm. H. Silverstein.

Practical Orthodontics for the General Practitioner. Nov. 8 and 9, 1961. Saul R. Kaye.

Tested Technics for Establishing Practice Growth. Nov. 8 and 9, 1961. Abraham Berliner.

Cosmetic Approach to Fixed Anterior Restoration. Nov. 10 and 11, 1961. David Shelby.

Fixed Bridges and Porcelain Restorations. Nov. 15 and 16, 1961. Harold Schwartz.

A Comprehensive Survey of the Acrylics in Dentistry. Nov. 17 and 18, 1961. A. Milton Bell.

Hospital Operating Room Technique for the General Practitioner. Nov. 29, 1961. (9 A.M. to 1 P.M., Grand Central Hospital, 321 E. 42nd St., New York, N. Y.) Bernard M. Cohen.

An Entirely New Approach to Full and Partial Denture Construction. Nov. 29 and 30, 1961. Jack M. Buchman and Harold Gelb.

Analgesia for Modern Dentistry. Nov. 30 to Dec. 2, 1961. Harry Langa.

Bite Planes, Provisional Ligatures and Splints. Nov. 30 to Dec. 2, 1961. Abraham Berliner.

Oral Reconstruction, Emphasizing Esthetics, Using Porcelain Jackets and Porcelain Fused to Gold. Dec. 1 and 2, 1961. Herbert H. Kabnick.

Removable Precision Bridge Techniques in Reconstruction Diagnosis and the Approach Treatment. Dec. 12 to 16, 1961. I. Franklin Miller.

All courses will be held from 10 A.M. to 4:30 P.M., unless otherwise noted, at the Statler Hilton, Seventh Ave. at West 33rd St., New York, New York.

For further information and application blank, please write to the Postgraduate Education Program, First District Dental Society, Statler Hilton, New York 1, New York.

University of Alabama

The School of Dentistry announces that Dr. Leonard Robinson will conduct a course in oral cancer, Dec. 9 to 11, 1961.

Further information may be obtained from the Director, Refresher Course Program, University of Alabama School of Dentistry, 1919 Seventh Ave., South, Birmingham 3, Alabama.

Boston University

The Department of Stomatology announces the following courses:

Occlusal Adjustment. Oct. 30 to Nov. 3, 1961. Bernard S. Chaikin, Henry M. Goldman, Gerald M. Kramer, William Pendergast, Irving Romanow, Morris Feder, and associates. $200.00.

Periodontal Therapy. Nov. 6 to 10, 1961. Henry M. Goldman, Bernard S. Chaikin, Gerald M. Kramer, William Pendergast, Jack Bloom, and associates. $200.00.

Endodontics. Nov. 13 to 17, 1961. Herbert Schilder. $175.00.

Fixed Bridge Prosthesis. Nov. 27 to Dec. 1, 1961. Leo Talkov, David J. Baraban, and Lloyd Warshauer. $175.00.

Special Week-end Course: Esthetics in Restorative Dentistry. Oct. 20 and 21, 1961. Charles L. Pincus. $75.00.

Albert Einstein College of Medicine, Yeshiva University

The Postgraduate Dental Program of the Albert Einstein College of Medicine of Yeshiva University announces the following postgraduate courses:

Anesthesiology DPD 15. April 12 and 13, 1962. Stanley R. Spiro and associates. $60.00.

Endodontics DPD 22. Feb. 22, March 1, and March 8, 1962. Julius Fox and associates. $100.00.

Endodontics DPD 25. Nov. 29, 1961. Julius Fox. $30.00.

Diagnostic Oral Pathology for Oral Surgeons DPD 28. Oct. 26 and 27, 1961. Ernest Baden and Surindar Bhaskar. $60.00.

Dental Alveolar Surgery DPD 33. May 3 and 4, 1962. William Rakower, Herbert Calman, Stanley J. Behrman, and associates. $60.00.

Periodontics DPD 69. Oct. 30 to Nov. 3, 1961. Irving Yudkoff, Marvin N. Okun, and associates. $175.00.

Periodontics DPD 66. Ten Wednesdays, beginning Feb. 28, 1962. Marvin N. Okun, Irving Yudkoff and associates. $225.00.

Pharmacology DPD 44. Jan. 25 and 26, 1962. Stanley R. Spiro and associates. $60.00.

Clinical Photography DPD 71. Nov. 16 and 17, 1961. Eugene B. Blanck. $50.00.

For application blanks and further information about specific postgraduate courses, write to Director, Postgraduate Dental Program, Albert Einstein College of Medicine, Yeshiva University, Eastchester Rd. and Morris Park Ave., Bronx 61, New York.

University of Illinois

The University of Illinois College of Dentistry is accepting applications for two- and three-year full-time courses in oral surgery, beginning July, 1962. Both programs carry credit toward a Master of Science degree.

Further information can be obtained from Dr. Daniel M. Laskin, Department of Oral and Maxillofacial Surgery, University of Illinois, 808 S. Wood St., Chicago 12, Illinois.

University of Kentucky

The College of Dentistry announces the following postgraduate courses for the fall of 1961:

Oral Diagnosis and Clinical Oral Pathology. Sept. 30, 1961. Stephen F. Dachi and associates.

Complete Denture Prosthetics for the General Practitioner. Oct. 2 to 4, 1961. William R. Laney.

Restorative Dentistry. Nov. 2 and 3, 1961. John H. Mosteller.

Periodontics for the General Practitioner. Dec. 4 to 6, 1961. Harry M. Bohannan.

Further information may be obtained from Dr. Stephen F. Dachi, Director of Postgraduate Education, College of Dentistry, University of Kentucky, Lexington, Kentucky.

New York University

The Department of Periodontia and Oral Medicine of the New York University College of Dentistry has announced a one-day basic course in "The Uses of Ultrasonics in Periodontal Therapy," to be given from 9:30 A.M. to 5:30 P.M. on Friday, November 17.

Applications for the course and additional information can be obtained by writing to Director, Postgraduate Division, New York University College of Dentistry, 421 First Ave., New York 10, New York.

University of Pennsylvania

The following postgraduate courses are announced:

Dermatologic Lesions With Oral Manifestations. Nov. 27 and 28, 1961. Jens J. Pindborg.

Handicapped Problems. Nov. 30, 1961. Manuel M. Album and associates.

The Use of Ultrasonics in Periodontia. Dec. 16, 1961. Henry M. Goldman and D. Walter Cohen.

Periodontal Histopathology. Jan. 8 to 12, 1962. Henry M. Goldman, D. Walter Cohen, and Frederic M. Chacker.

Practical Procedures of Oral Rehabilitation. Part I. Jan. 15 to 19, 1962. Ernest R. Granger, William Maxwell, and Robert Simpson.

Orthodontic Treatment Planning and Associated Appliance Therapy. Jan. 22 and 23, 1962. William L. Wilson.

Cephalometry. Jan. 22 to 25, 1962. Viken Sassouni.

Impacted Teeth. Jan. 24 to 26, 1962. Victor H. Frank and associates.

Periodontal Prosthesis. Feb. 5 to 9, 1962. Morton Amsterdam and D. Walter Cohen.

Partial Dentures. Feb. 26 to March 2, 1962. M. M. DeVan and associates.

For further information, please write Postgraduate Courses, School of Dentistry, University of Pennsylvania, 4001 Spruce St., Philadelphia 4, Pennsylvania.

University of Pittsburgh

Applications are now being accepted by the Graduate Division of the School of Dentistry for graduate study in the fields of anesthesiology, oral surgery, orthodontics, periodontics, and prosthodontics, leading to Master of Science degrees. Selection of students for the fall session of 1962 will be made in March, 1962.

A nondegree, full-time, twelve-month course in general anesthesia is also available for qualified dental graduates.

Graduate study in the preclinical basic sciences of anatomy, biochemistry, microbiology, pathology, pharmacology, and physiology, leading to Master of Science or Doctor of Philosophy degrees, is also offered. Successful applicants in this latter program are eligible for financial assistance in the form of traineeships.

For further information and application forms, write to Director of Graduate Education, University of Pittsburgh, School of Dentistry, Pittsburgh 13, Pennsylvania.

Temple University

The School of Dentistry announces the following graduate and postgraduate courses:

Dental Roentgenology. Oct. 12 and 13, 1961. Sydney Blackman. $50.00.
Clinical Endodontics Seminar. Oct. 20, 1961. Leonard Parris. $35.00.
Clinical Endodontics. Nov. 6 to 11, 1961. Leonard Parris and associates. $200.00.
High Speed in Operative Dentistry. Dec. 13, 1961. Carlos Weil and Charles A. Nagle, Jr. $35.00.
Implant Dentures. Jan. 8 to 12, 1962. Aaron Gershkoff and Norman I. Goldberg. $200.00.
Periodontal Prosthesis. Feb. 5 to 9, 1962. Morton Amsterdam and D. Walter Cohen. $275.00.
Pedodontics for the General Practitioner. Feb. 12 to 16, 1962. Ernest F. Ritsert. $175.00.
Practice Administration. Feb. 17, 1962. Jay H. Eshleman. $25.00.
Advanced Fixed Prosthesis. Feb. 19 to 24, 1962. George Straussberg. $200.00.
Electronic Electrosurgery. March 7 and 8, 1962. Maurice J. Oringer. $60.00.
Transographics Seminar. March 30 and 31, 1962. William A. Miller. $75.00.
Immediate Surgical Endodontics. April 2 to 6, 1962. Leonard Parris, Harold Rappaport, and Robert Uchin. $200.00.
Advanced Surgical Techniques in Periodontal Therapy. April 9 to 13, 1962. Saul Schluger and Jack Alloy. $300.00.
Full Denture Seminar. May 5, 1962. Bernard Jankelson. $30.00.
Full Denture Prosthesis. May 7 to 11, 1962. Bernard Jankelson. $200.00.
Graduate Orthodontics. Robert B. Hedges and associates. $450.00 per semester.

For application and further information, write to Dr. Louis Herman, Director of Postgraduate Studies, Temple University School of Dentistry, 3223 North Broad St., Philadelphia 46, Pennsylvania.

University of Texas

"Conceptual Advances in Immunology and Oncology" will be the subject of the sixteenth annual Symposium on Fundamental Cancer Research, to be held March 1 to 3, 1962.

Further information on the meeting may be obtained from the Publications Department, The University of Texas M. D. Anderson Hospital and Tumor Institute, Texas Medical Center, Houston 25, Texas.

Tufts University

The School of Dental Medicine announces the following postgraduate courses:

201A. Cancer of the Oral Cavity and Salivary Glands. Six Thursdays, beginning Oct. 6, 1961. Gerald Shklar, Irving Meyer, and staff. $125.00.
301A. Hospital Management of the Dental Patient. Feb. 7 to 9, 1962. Richard Taylor and Dental Department of Boston City Hospital. $100.00.
300A. A Participation Course in Applied Anatomy of the Head and Neck. Feb. 28 to March 2, 1962. Alton D. Brashear and Dental Department of Boston City Hospital. $100.00.

202A. The Diagnosis, Management and Therapy of Lesions of the Oral Mucosa. Eight Wednesdays, March 7 to April 25, 1962. Philip McCarthy, Francis P. McCarthy, and Gerald Shklar. $125.00.

200A. Surgical Pathology of the Mouth and Jaws. Eight Thursdays, March 8 to May 10, 1962. Irving Meyer, Gerald Shklar, and staff. $125.00.

606A. A Special Participation Course in Periodontology. April 9 to 13, 1962. Irving Glickman and department staff. $175.00.

302A. Minor Oral Surgery. May 8 to 10, 1962. Richard Taylor and staff of Boston City Hospital. $125.00.

For further information concerning these courses please write to Dr. L. Walter Brown, Jr., Director, Post-Graduate Refresher Courses, Tufts University School of Dental Medicine, 136 Harrison Ave., Boston 11, Massachusetts.

Medical College of Virginia

The following postgraduate courses will be presented:

Dental Therapeutics. March 5 to 7, 1962 (at the Williamsburg Lodge, Williamsburg, Virginia). F. B. Wiebusch, H. M. Syrop, and D. H. Bell. $125.00, including single room and meals for three days.

Anatomy of the Head and Neck. March 12 to 16, 1962. A. D. Brashear. $75.00.

Oral Surgery. April 2 to 4, 1962. S. E. Bear, W. J. Longan, and P. B. Peters. $75.00.

Removable Partial Dentures. April 3 to 5, 1962. D. H. Bell, F. W. Salisbury, and C. M. Heartwell. $75.00.

Complete Denture Prosthesis. April 6 to 8, 1962. C. M. Heartwell, D. H. Bell, and F. W. Salisbury. $75.00.

Clinical Photography. April 9, 1962. M. C. Shaffer and P. J. Modjeski. $25.00.

Oral Roentgenology. April 11 to 13, 1962. L. D. Mitchell, Jr., and C. D. Richardson. $75.00.

For further information, write to Dr. H. T. Knighton, Director of Postgraduate Instruction, Medical College of Virginia, School of Dentistry, Richmond 19, Virginia.

University of Washington

King County Hospital System announces that a residency in oral surgery will be available starting July 1, 1962.

Training includes oral surgery, general anesthesia, radiology, and pathology. The residency is approved by the American Dental Association and is supervised by the University of Washington Oral Surgery Department.

Application forms and information may be obtained by writing to Oral Surgery Service, King County Hospital System, 325 Ninth Ave., Seattle, Washington.

REVIEWS OF THE LITERATURE

BOOK REVIEW

Die Begutachtung in der Zahn-, Mund- und Kieferheilkunde (Professional Opinions in Dentistry). Prof. Dr. Theodor Kirsch. Heidelberg, 1961, Dr. Alfred Hüthig Verlag. 496 pages, 709 illustrations. Price, DM 40.

This is an interesting and unusual book which deals with the technique of examination and the rendering of scientific, professional, and legal opinions in cases of complaints that may be based on procedures performed by general dentists or dental specialists which were not executed *leges artis* or which resulted in complications. The book is based on the experience of the author and includes illustrative case reports and references to the literature dealing with the problem.

K. H. T.